

February-April 2022

# LIVING WITH CANCER



## COLORECTAL CANCER RESEARCH & PRACTICE UPDATES

Colorectal Cancer Canada curates monthly Research & Practice Updates to inform patients and their loved ones of new innovations in colorectal cancer care. The following updates extend from February 1<sup>st</sup> 2022 to April 30<sup>th</sup>, 2022 inclusive and are intended for informational purposes only

### FEBRUARY-APRIL 2022 PREVIEW

Can weight loss in adulthood reduce the risk of developing colorectal polyps?.....	2
High response rate seen with nivolumab added to encorafenib and cetuximab in BRAF V600E-mutated mCRC.....	5
Association between unprocessed red meat and processed meat with risk of recurrence and mortality in CRC.....	7
Alcohol intake and risk of alcohol-related cancer.....	7
Study finds taller adults may be at increased risk for colorectal cancer.....	7

## Can weight loss in adulthood reduce the risk of developing colorectal polyps?

February 2022

While obesity is a known risk factor for colorectal cancer (CRC), the impact of weight change on the development of adenomas, a type of precancerous polyp, is not well understood. A new study published in *JNCI Cancer Spectrum* found that weight loss among adults, particularly for those who are overweight or obese, may reduce their risk of developing adenomas. The researchers found that losing at least two pounds per decade from early to late adulthood until the mid-70s reduced an individual's risk for developing adenomas by 46%. Among individuals who were overweight or obese at age 20, weight loss was associated with a more than 60% reduction in risk.

### The Study

The researchers evaluated 17,629 participants from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening trial who had available weight data, reported no history of colorectal polyps or other predisposing colon conditions, had received a negative screening test result for polyps or CRC at the start of the trial, and received a follow-up sigmoidoscopy 3-5 years later. Weight loss in adulthood was linked to reduced adenoma risk, whereas weight gain greater than 3kg every 5 years increased risk. These findings underline the importance of maintaining a healthy weight throughout adulthood to help prevent the development of colorectal adenomas.

### Take away message:

Weight loss in adults, particularly among those who are overweight or obese, appears to reduce the risk of developing adenomas, a type of precancerous growth that may become colorectal cancer.

[READ THE ARTICLE](#)

## High response rate seen with nivolumab added to encorafenib and cetuximab in BRAFV600E-mutated mCRC

February 2022

Findings from a phase I/II trial showed that the combination of a BRAF inhibitor (encorafenib) plus an EGFR inhibitor (cetuximab) and immunotherapy (nivolumab) produced a positive response rate and high disease control rate in patients with microsatellite stable (MSS) BRAFV600E-mutated metastatic colorectal cancer (mCRC).

***Microsatellite instability high (MSI-H):*** a biomarker that describes the condition of a tumour having a high likelihood of developing mutations, resulting from impaired DNA mismatch repair (MMR). A

tumour that is MSI-H is characterized by a high number of mutations. This biomarker is present in about 5% of CRCs and is a predictor for positive response to immunotherapy.

**Microsatellite stable (MSS):** a biomarker that describes the condition of a tumour having a normally functioning DNA mismatch repair (MMR). The majority (95%) of CRCs are MSS. MSS tumours are characterized by low “detectability” by the body’s immune system, which means that these tumours are not responsive to immunotherapy.

**BEACON CRC study:** a landmark trial that established the combination therapy of a BRAF inhibitor (encorafenib) plus an EGFR inhibitor (cetuximab) as the standard of care for patients with BRAFV600E-mutated metastatic colorectal cancer.

In the study, patients with MSS BRAFV600E mCRC who had received one or two previous lines of therapy but no prior immunotherapy were enrolled in the study. The triplet combination of immunotherapy (nivolumab) plus encorafenib and cetuximab proved to be an effective and promising treatment in the context of the previously reported results from the BEACON CRC study, resulting in a 50% overall response rate, with all patients achieving at least a partial response. The disease control rate was 96% among the 22 patients enrolled in the study. Furthermore, the combination therapy was well-tolerated by patients with no toxicities that caused patients to need to stop treatment.

The investigators concluded that the combination of encorafenib, cetuximab, and nivolumab appears to be a safe and well-tolerated treatment for patients with MSS BRAF-mutated mCRC.

### Take away message:

Findings from a phase I/II clinical trial showed that the addition of immunotherapy (nivolumab) to the combination of targeted therapies encorafenib and cetuximab produced a high response rate and an acceptable safety and toxicity profile among patients with previously treated, microsatellite stable, BRAF V600E-mutated metastatic colorectal cancer.

[READ THE FULL ARTICLE](#)

### Associations between unprocessed red meat and processed meat with risk of recurrence and mortality in patients with stage III colon cancer

February 2022

A recent study published in *JAMA Network Open* investigated whether consumption of unprocessed red meat or processed meats such as bacon, ham, or smoked meats after diagnosis were associated with a higher risk of recurrence and death in patients with colon cancer. Both the American Cancer Society and the American Institute for Cancer Research recommend that cancer

survivors limit intake of red and processed meats – a recommendation that is based on solid associations that have been found between red and processed meat intake and cancer risk, especially risk of colorectal cancer. However, there is little data on the impact of red and processed meat intake on cancer outcomes *after* diagnosis.

### The study

The study used data from participants with stage III colon cancer who were enrolled in the Cancer and Leukemia Group B (CALGB 89803/Alliance) trial which took place between 1999 and 2001. Unprocessed red meat and processed meat intake were assessed using a validated food questionnaire during and 6 months after chemotherapy. The investigators found that intake of unprocessed red meat or processed meat after colon cancer diagnosis was not associated with a greater risk of cancer recurrence or death. Key limitations of the study that should be considered include the fact that it depended on self-reported dietary behaviour, which may not capture patient data very accurately. Additionally, the study only examined data from patients with stage III colon cancer, which means that the results may not be applicable patients with other stages of the disease. Further studies are needed to investigate this association in larger and more diverse patient populations.

### Take away message:

While consumption of unprocessed red meat and processed meats has been shown to be associated with an increased risk of developing cancer, particularly colorectal cancer, a recent study found that consumption of red and processed meats after cancer diagnosis does not appear to increase risk of cancer recurrence or death.

[READ THE FULL ARTICLE](#)

### Alcohol intake and risk of alcohol-related cancer

March 2022

A new study from Australia found that heavy drinking in early adulthood may increase the risk for alcohol-related cancers, including colorectal cancer (CRC), even after drinking decreases or stops entirely in middle age.

Alcohol is a known risk factor for CRC – the 2018 [World Cancer Research Fund and American Institute for Cancer Research report](#) (“Diet, nutrition, physical activity and colorectal cancer”) states that there is strong evidence to show that consuming approximately 2 or more alcoholic drinks per day increases the risk of developing CRC<sup>1</sup>. The precise mechanisms that drive the association between alcohol consumption and cancer development are not fully understood, though a large body of evidence has shown that the toxic by-product produced in the body when

alcohol is consumed - acetaldehyde – interferes with DNA synthesis and repair, and therefore may contribute to the development of cancer<sup>1</sup>.

In the study, researchers analyzed individuals' lifetime drinking trajectories and risk for alcohol-related cancer using data from the Melbourne Collaborative Cohort Study which involved 22,756 women and 15,701 men. Heavy drinking was defined as an average alcohol intake of at least 60g/day, which is about the equivalent of 6 standard alcoholic drinks. For men, compared to non-drinkers, heavy drinking trajectories were associated with an increased overall risk for alcohol-related cancer, with the strongest associations for the early decreasing heavy trajectory (individuals who started as heavy drinkers at age 20-39 ( $\geq 60$  g/day) and continued to cut down their intake over time until arriving at stable, light drinking habits by age 60-69), and the late decreasing heavy trajectory (individuals who started drinking  $\geq 60$  g/day in their 20s and began to decrease their intake from age 60-69).

For women, the increasing moderate trajectory (individuals who consumed around 20g/day (2 alcoholic drinks) at age 20-29 and gradually increased their alcohol intake over time to consume close to 40g/day (4 alcoholic drinks) by age 50-59) was associated with the greater risk for alcohol-related cancer overall. The increasing moderate trajectory in women was similarly associated with an increased risk for breast and colorectal cancer.

These findings demonstrate the impact of heavy drinking on cancer risk even when drinking decreases or stops completely later in life. The study investigators concluded that while the WCRF/AICR report underlines the importance of limiting alcohol intake during middle age to prevent cancer, the study findings highlight the additional importance of limiting alcohol intake during early adulthood.

### **Take away message:**

While there is a known association between alcohol consumption and the development of cancer, a recent study highlights the association between cancer and alcohol consumption not just in middle age but during early adulthood.

[READ THE FULL ARTICLE](#)

### **Study finds taller adults may be at increased risk for colorectal cancer**

March 2022

New research on the association between taller individuals and colorectal cancer found that taller adults may be more likely to develop colon polyps or colorectal cancer compared to shorter adults. A possible reason for the association involves body organ size, where more active cell

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<sup>1</sup> <https://www.wcrf.org/wp-content/uploads/2021/02/Colorectal-cancer-report.pdf>

proliferation in organs of taller people could result in a greater possibility of mutations leading to cancer development.

Using data from 47 international, observational studies and adjusting for demographic, socioeconomic, behavioural and other known risk factors of colorectal cancer, the study findings suggest that individuals within the highest percentile of height had a 24% higher risk of developing colorectal cancer than the shortest individuals in the lowest percentiles of height. Each 10cm increase in height was found to be associated with a 14% increased risk of developing colorectal cancer, and a 6% increased chance of developing colorectal adenomas (polyps). The researchers concluded that more studies are needed to determine at which height earlier colorectal cancer screening would be warranted.

**Take away message:**

Findings from a recent study found that taller adults are more likely to develop colorectal cancer or colorectal polyps compared to shorter adults. More research is needed to determine at which height earlier colorectal cancer screening would be warranted.

[READ THE FULL ARTICLE](#)