

COLORECTAL CANCER CARE AND PREVENTION

COLON CANCER

The colon, or large intestine, connects the small intestine to the anus and includes the ascending colon, transverse colon, descending colon, rectum, and anus. Cancer can form anywhere along this tract. Most colorectal cancers begin as a polyp, which can be detected during routine screening colonoscopy performed every 10 years starting at age 45. Other forms of screening include an annual stool fecal immunochemical (FIT) test, virtual CT colonography every 5 years, or Cologuard stool DNA test every 3 years.

From the time the first abnormal cells start to grow into polyps, it takes 10 to 15 years for them to develop into colorectal cancer. Adenomatous polyps have a higher rate of turning into cancer, while hyperplastic and inflammatory polyps are typically not precancerous.[1] The lifetime risk of developing colorectal cancer is about 1 in 24 (4.2%), and it is 60% more common in developed countries. This risk is slightly lower in women than in men, but it is the third leading cause of cancer and second leading cause of cancer-related deaths.[2] Up to 70% of colorectal cancers can be prevented by diet and lifestyle changes.[3]

RISK FACTORS FOR COLON CANCER

INCREASE RISK:

- Age greater than 45
- African American race
- Personal or family history of adenomatous polyps or colon cancer
- Inflammatory bowel disease (Crohn's or ulcerative colitis)
- Genetic syndromes: Familial adenomatous polyposis or hereditary nonpolyposis colon cancer, and others
- Type 2 diabetes
- Obesity[4-6]
- Smoking and high alcohol use
- Red and processed meats[7-9]

DECREASE RISK:

- High-fiber diet[10,11] consisting of fruits[12], vegetables (especially cruciferous),[13,14] and omega-3 fats[15]
- Moderate exercise 150 minutes per week or vigorous exercise 75 minutes per week[16,17]
- Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs)[18]

ASPIRIN AND NSAIDS

The chemopreventive effect of aspirin and NSAIDs has been attributed to their inhibition of cyclooxygenase (COX) enzymes. COX-2 is abnormally expressed in many cancer cell lines and implicated in the process of carcinogenesis, tumor growth, apoptosis, and angiogenesis. Studies indicate that regular aspirin use of 75 mg or more for greater than 5 years leads to a 20% to 30% reduction in colon cancer incidence.[19] Daily aspirin use of 81 to 325 mg reduces the occurrence of tubular adenomas in those with a history of them.[20,21] However, NSAID use prior to diagnosis does not affect survival in colon cancer patients.[22] An international consensus determined that more studies of aspirin and cancer prevention are needed to define the lowest effective dose, the age at which to initiate therapy, the optimum treatment duration, and the subpopulations for which the benefits of chemoprevention outweigh the risks of adverse side effects.[23]

NONPHARMACOLOGICAL THERAPIES FOR THE PREVENTION AND TREATMENT OF COLON CANCER

FOOD AND DRINK

Part of the reason for the difference in colorectal cancer incidence in other countries compared to the United States is the difference in diet. People in other countries, especially Asia, tend to have a diet higher in fiber, fish, and vegetables and lower in red meat and processed foods.

FIBER

Increased fiber in the diet contributes to a lower incidence in colon cancer, with dietary fiber, cereal fiber, and whole grains having the greatest reduction. A linear inverse relationship indicated that every 10 gm of fiber intake results in a 10% risk reduction for colon cancer.[10] Another analysis found no association between fiber intake and rectal cancer incidence.[24] It is recommended to consume at least 30 gm of dietary fiber a day.

FISH & OMEGA-3 FATTY ACIDS

Omega-3 fatty acids are found in cold water, oily fish. Their activity against colorectal cancer involves modulation of COX-2 activity, alteration of membrane dynamics and cell surface receptor function, increase in oxidative stress, and the creation of novel anti-inflammatory lipid mediators.[25] Studies have shown varied results regarding the influence of omega-3 fatty acids on colorectal cancer risk.[26,27] Due to the amount of mercury in fish, no more than 2 to 3 servings of cold-water fish are recommended per week. Fish high in omega-3 fatty acids are wild salmon, mackerel, sardines, anchovies, black cod, and albacore tuna. The omega-3 fatty acid content of 100 gm of salmon and sardines is between 1 and 2 gm. One may also consider taking 1,000 mg of omega-3 fatty acids daily in supplement form. For more information, refer to [*Passport to Whole Health*](#) Chapter 8 “The Anti-Inflammatory Diet”.

SOY

Soy foods consist of soy beans (edamame), tofu, tempeh, miso, and soy milk and are a common part of the Asian diet. There is no connection between soy consumption and reduction in risk of colorectal cancer. However, men and women are looked at separately, soy consumption is associated with a 21% risk reduction in females, but not in males.[28]

RED AND PROCESSED MEAT

Higher consumption of red meat is linked to an increased risk of colorectal cancer, with processed meats contributing to a greater risk.[8,9] There is a 36% increased risk in colorectal cancer for every 100 gm/day intake of red meat and 28% increased risk for every 50 gm/day intake of processed meat.[8] Heterocyclic amines and polycyclic aromatic hydrocarbons, which form during frying and barbecuing meats, are carcinogenic. The heme-iron content of meats may contribute to colorectal neoplasia by inducing oxidative DNA damage and by increasing endogenous formation of N-nitroso compounds that are also carcinogens. Red meat intake is associated with risk of large adenomas.[9] Processed meats include most lunchmeats found in deli counters, anything with a casing or in sausage form, and anything smoked or cured like bacon. Advise choosing other sources of protein or baking, boiling, pressure-cooking and slow-cooking unprocessed meats instead.

GARLIC

Garlic (*Allium sativum*) is characterized by a high content in organosulfur compounds and flavonoids, and can be consumed raw or cooked. The allyl sulfur constituents in garlic, which comprise of 1% of its dry weight, are responsible for its health benefits. Its anticancer properties include blockage of cell growth, proliferation, and angiogenesis; apoptosis induction; and inhibition of COX-2 expression. Several studies show that a high consumption of garlic decreases the risk of colorectal cancer by 30%, with a greater protective effect on the distal colon.[29,30]

GLYCEMIC CONTROL

Impaired glycemic control is the result of a diet high in simple carbohydrates (fructose and sucrose), which leads to diabetes and hypertriglyceridemia. There is mixed evidence to support an association between glycemic index, glycemic load, and colorectal cancer risk.[31,32] Every 20 mg/dL increase in fasting blood glucose is associated with a 1.5% increased incidence of colon cancer. [33] It is advisable to reduce dietary simple carbohydrates (white and wheat flour products) and refined sugar due to their association with many other chronic diseases that can result in heart attack and stroke.

MEDITERRANEAN DIET

The principal aspects of this diet include proportionally high consumption of olive oil, legumes, unrefined cereals, fruits, and vegetables; moderate to high consumption of fish; moderate consumption of dairy products (mostly as cheese and yogurt); moderate wine consumption; and low consumption of meat. A European study found that adherence to the

Mediterranean diet is associated with an 8% to 11% risk reduction in colorectal cancer. This association was stronger in women and not affected by alcohol intake.[34]

OBESITY

Obesity is defined as a BMI of 30 or greater, and is a risk factor for many solid tumors and chronic diseases. Abdominal obesity, measured by hip and waist circumference, is closely associated with adverse metabolic profiles such as insulin resistance, dyslipidemia, and systemic inflammation, which contribute to cardiovascular disease, diabetes, and certain types of cancer. Studies show that both general and central obesity are associated with an increased risk of colorectal cancer, with a stronger association in men.[5,6] Childhood obesity and weight change in adulthood may also be associated with colorectal cancer risk. Advise maintaining a BMI between 21 and 25.

DIETARY SUPPLEMENTS

Note: Please refer to the [Passport to Whole Health](#), Chapter 15 on Dietary Supplements for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

CALCIUM

Supplemental calcium is effective for the prevention of colorectal adenoma recurrence in populations with a history of adenomas.[35-39] The number needed to treat is 20 to prevent one colorectal adenoma recurrence within a period of 3 to 5 years.[40] Food sources of calcium include dairy, white beans, bone-in sardines, kale, black-eyed peas, dried figs, seaweed, tofu, and soymilk.

Dose: 1,200 mg calcium citrate daily. Calcium citrate is better absorbed than calcium carbonate and with less gastrointestinal effects.

VITAMIN D

Vitamin D may decrease cancer risk by improving differentiation and apoptosis and decreasing proliferation, invasiveness, metastatic potential, and angiogenesis. There is an inverse association between circulating 25(OH)D levels and colorectal cancer, with a stronger association for rectal cancer.[41-43] A 50% lower risk of colorectal cancer was associated with a serum 25(OH)D level greater than or equal to 33 ng/mL, compared to less than or equal to 12 ng/mL.[44]

Dose: Target 25(OH)D level between 50 and 80 ng/mL. Every 1,000 IU of vitamin D3 will raise the level by 8 to 10 ng/mL.

FOLATE

Folic acid is a type of B vitamin. It is the synthetic form of folate that is found in supplements and added to fortified foods. The association between folate, folic acid, and colorectal cancer is mixed. Some studies have found that a higher intake of folate in the diet and in folic acid supplements is associated with a reduced risk of colorectal cancer.[45-47] Other studies show no association at all for prevention or reducing the recurrence of colorectal cancer.[48-51] Finally, two studies found an increased risk of colorectal cancer incidence and recurrence in those supplementing with folic acid.[52,53] Rather than supplementing with folic acid, it is advisable to obtain folate from food sources which include lentils, most beans, asparagus, spinach, avocados, broccoli, and oranges.

Dose: Methylfolate 400-1000 mcg per day.

VITAMIN B6

In the United States, the prevalence of inadequate vitamin B6 intake for adults older than 45 years is about 20% for men and 40% for women. Vitamin B6 intake and blood pyridoxal 5'-phosphate levels are inversely associated with the risk of colorectal cancer, with a 20% decreased risk when comparing high versus low intake.[54] Overall, the risk of colorectal cancer decreases by 49% for every 100-pmol/mL increase in blood pyridoxal 5'-phosphate level. Food sources of vitamin B6 include garlic, tuna, cauliflower, mustard greens, bananas, celery, cabbage, cremini mushrooms, asparagus, broccoli, kale, collard greens, Brussels sprouts, cod, and chard.

Dose: 50 mg daily or in a multivitamin.

CURCUMIN

Curcumin is a compound extracted from turmeric (*Curcuma longa*), a yellow Indian spice. The bioavailability of curcumin consumed orally increases when it is taken with black pepper (piperine) and a healthy fat. A small open-label trial showed a 60% reduction in colorectal adenoma number and 50% reduction in size in patients with familial adenomatous polyposis (FAP) who took 1,440 mg of curcumin with quercetin daily for 6 months.[55] Another open-label trial found a 40% reduction in aberrant crypt foci in smokers who took 4 gm as opposed to 2 gm of curcumin daily for 30 days prior to colonoscopy.[56] Curcumin can cause blood thinning, so use with caution in patients with a low platelet count or taking other herbs that thin the blood. It may cause gastrointestinal discomfort, so titrate the dose up slowly.

Dose: 1.5-4 gm in divided doses per day for anti-inflammatory benefits. More research is needed regarding colorectal cancer prevention. May cause bruising and increase risk of bleeding, consider avoiding if hemoglobin is less than 10 or platelets are less than 100.

MOVING THE BODY

Physical activity reduces the incidence of colon but not rectal cancer. There is a 30% to 50% risk reduction in people with the highest level of physical activity, with a stronger reduction in left-sided cancers.[57] Increased physical activity after the diagnosis of stage I to III or advanced colon cancer reduces cancer-related mortality. Additionally, there is a reduction in colon cancer recurrence or death in people with the highest level of physical activity 6 months after chemotherapy. This is independent of other lifestyle factors and walking at a normal or brisk pace for 30 minutes or more daily is effective.[58] Patients who have received chemotherapy that can affect heart function should take extra precautions and talk to their doctor before starting a vigorous exercise program.

SUMMARY

Lifestyle modifications are imperative to prevent colorectal cancer. The top modifiable risk factors include exercising 30 minutes most days of the week and adapting a high-fiber diet with five to nine servings of fruits and vegetables per day. Adding garlic, soy, and omega-3 fats to the diet while reducing red meat, processed meat, and simple carbohydrates can have added benefit in the prevention of colorectal cancer. For average-risk patients, screening should start at age 45 with colonoscopy every 10 years, sigmoidoscopy every 5 years, or annual fecal occult blood testing for early detection of precancerous lesions. An anti-inflammatory diet with regular exercise is beneficial for colorectal cancer prevention.

RESOURCE LINKS

- [Colorectal Cancer Alliance](https://www.ccalliance.org/): <https://www.ccalliance.org/>
- [Fight Colorectal Cancer](https://fightcolorectalcancer.org/): <https://fightcolorectalcancer.org/>
- [Passport to Whole Health](https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport_to_WholeHealth_FY2020_508.pdf): https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport_to_WholeHealth_FY2020_508.pdf

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