Beyond Conventional Cancer Therapies

Colorectal Cancer

February 2021

A Handbook of

Integrative Cancer Care Options

and the Research Behind Them

BCCT Colorectal Cancer Handbook

Updated February 2021

Key Points

- Early detection, allowing for early treatment, is very important with colorectal cancer.
- Eating Well and Moving More, two of our 7 Healing Practices, pack a powerful one-two punch in potentially improving treatment outcomes, enhancing quality of life and/or reducing risk of recurrence in colorectal cancer.
- Conventional treatments are readily available. Complementary therapies can be useful to enhance conventional treatment effects, improve quality of life and possibly even extend life for those with colorectal cancer.
- An observational study and a case study provide examples of integrative approaches. See Examples of Integrative Approaches.
- A number of natural products; off-label, overlooked, or novel cancer approaches (which we call ONCAs); and other therapies show benefits in four domains:
    - Treating the cancer
    - Managing side effects and promoting wellness
    - Reducing risk of both cancer onset and recurrence
    - Optimizing your body terrain
- The microbes in your gut influence colorectal cancer development and might influence the success of treatment.
- Choices for pain relief during and after surgery can impact treatment outcomes and risk of recurrence.

Contents

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February 2021

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Quick Reference to Integrative Therapies

Top approaches by effectiveness and safety.

7 Healing Practices

Moving More

- Participate in regular physical activity to reduce risk, promote survival and reduce side effects including fatigue and nausea.

Managing Stress

- Follow stress-reducing therapies such as mind-body approaches.

Sleeping Well

- Sleep 7 to 9 hours at night (or more if needed during treatment).
- Sleep at night and not during the day if possible.

Sharing Love and Support

- Establish sources of emotional support and reassurance for yourself if possible.

Exploring What Matters Now

- Making sense of your cancer experience is related to higher quality of life.

Eating Well

To **reduce risk** or **promote survival** after diagnosis:

- A plant-based diet with a variety of fruits, vegetables, beans and whole grains can lower risk.
- Eat foods rich in omega-3 fatty acids and anti-inflammatory components such as these:
  - Deep orange vegetables
  - Fish and fish oil
  - Flaxseed oil
  - Garlic
  - Onions
  - Tea
  - Turmeric
  - Walnuts
- Eat foods high in calcium, folate, and vitamins B_2 and B_{12}, such as broccoli and other brassicas; chickpeas, kidney beans and other legumes; eggs, milk and plain yogurt.
- Eat foods rich in fiber, such as whole grains, many fruits and vegetables and legumes such as chickpeas, black beans or lentils.
- Eat foods rich in vitamin C, such as oranges, black currants, kiwifruit, mangoes, broccoli, spinach, bell peppers and strawberries.
- Limit or eliminate consumption of red and processed meat, especially for colon cancer.

To **reduce side effects and symptoms**:

- Almonds or cashews
- Black beans
- Dark chocolate
- Peanuts
- Pumpkin seeds
- Soy milk
- Spinach
- Whole-wheat foods

- Foods high in magnesium for peripheral neuropathy:
- A balanced diet rich in B vitamins (including B_1, B_{12} and folic acid, see above) and antioxidants to reduce pain from peripheral neuropathy

Creating a Healing Environment

- Avoid exposures to these agents known to increase colorectal cancer risk:
  - 1,1-dichloroethane
  - Alachlor
  - Aromatic amines
  - Chlorination byproducts
  - Ionizing radiation
  - Night-shift work
  - Nitrates in water
  - Solvents

See BCCT.ngo for more details about benefits and cautions regarding each therapy.

Natural Products

Treating the Cancer

- **Medicinal mushrooms**: turkey tail mushrooms or extracts, shiitake mushroom extracts
- Vitamin D

Managing Side Effects & Promoting Wellness

- **Astragalus**
- **Curcumin**
- Ginger
- **L-glutamine (glutamine)**
- Medical cannabis and cannabinoids
- Melatonin
- **Omega-3 fatty acids**
- **Probiotics**

Reducing Risk

- Calcium supplements
- Magnesium supplements
- Vitamin B_2 supplements
- **Medicinal mushrooms**: reishi mushrooms, turkey tail mushrooms or extracts

Optimizing Your Body Terrain

- Aged garlic extract
- **Astragalus** and other saponins
- **Curcumin**
- Green tea extracts/ EGCG
- **L-glutamine**
- **Omega-3 fatty acids**
- **Probiotics**
- Vitamin E supplements

Therapies listed as **Optimizing Your Body Terrain** create an environment within your body that does not support cancer development, growth or spread. These therapies may reduce inflammation, act as antioxidants, improve anticancer immune function, reduce glycemia or influence genetic expression, among other effects.

Other Approaches

For treating the cancer:

- Hyperthermia (both loco-regional and whole-body hyperthermia)

For managing side effects:

- **Acupuncture and electroacupuncture**
- Short-term fasting
- Guided imagery

For optimizing your body terrain:

- **Acupuncture and electroacupuncture**

Items in bold are listed for more than one therapeutic impact, and those in green are in all four.

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

Off-label drugs require a prescription and medical supervision and monitoring from a licensed physician.

Treating the Cancer

- **Aspirin** (noting cautions)
- **Chronomodulated therapies**
- **Metformin**
- Statins (noting cautions)

Managing Side Effects and Promoting Wellness

- **Chronomodulated therapies**
- **Metformin**

Reducing Risk

- **Aspirin** (noting cautions)
- **Metformin**
- Thiazolidinediones (TZDs)

Optimizing Your Body Terrain

- **Aspirin** (noting cautions)
- Cimetidine (Tagamet HB)
- **Metformin**
- Rapamycin (sirolimus)

Conventional Therapies

Conventional therapies for treating the cancer and managing side effects are widely available; ask your doctor for information about these:

- Surgery
- Radiofrequency ablation
- Cryosurgery
- Chemotherapy
- Radiation therapy
- Targeted therapy
- Immunotherapy

Creating Healthy Habits

For treating the cancer / promoting survival (the first two) and reducing risk (all four):

- **Achieve and maintain a healthy body weight.**
- **Limit alcohol consumption.**
- Eliminate tobacco use.
- Limit night shift work.

See BCCT.ngo for more details about benefits and cautions regarding each therapy.

Colorectal cancer is a term used to include several types of cancers of the colon and/or rectum. Common types of colorectal cancers:1

- Adenocarcinomas of the colon and rectum
- Gastrointestinal carcinoid tumors
- Primary colorectal lymphomas
- Gastrointestinal stromal tumors
- Leiomyosarcomas
- Melanomas of the colon or rectum

The evidence presented here for screening, diagnosis, treatment and reducing risk relates to carcinomas, of which the great majority are adenocarcinomas. The other cancer types are much less common, and behave quite differently.

Colorectal cancer begins when healthy cells in the lining of the colon or rectum change and grow out of control. These cells form a mass called a tumor, which can be cancerous or benign. A cancerous tumor is malignant, meaning it can grow and spread to other parts of the body. A benign tumor can grow but will not spread. These changes usually take years to develop.2

Of cancers that affect both men and women, colorectal cancer is the second leading cancer killer in the United States. It is most often found in people who are 50 years old or older.4 However, incidence is increasing in younger adults and declining in older age groups.5

There are many possible reasons for the fewer early-stage diagnoses in adults under 50, such as these:

- Younger adults may be less likely to report symptoms promptly or to have medical insurance than older adults, which may lead to initial diagnosis at a later stage.6
- Younger adults may also present more often with symptoms outside the national referral guidelines, leading to fewer prompt referrals for colorectal cancer assessment.7

Early detection, allowing for early treatment, is very important with colorectal cancer. Treatment is often most effective in small localized cancer. When the cancer is diagnosed in advanced stages, it is often not operable, which often means a lower chance of survival.8 Suggestions for detecting cancer early:

- Follow all screening guidelines, such as from What Should I Know About Screening? from the Centers for Disease Control and Prevention (also see at right).
- If you have a family history or any symptoms of colorectal cancer, ask your physician about more aggressive screening.

Colorectal Cancer: Signs, Symptoms and Screening

Signs and symptoms from the American Cancer Society:3

- A change in bowel habits—such as diarrhea, constipation or narrowing of the stool—that lasts for more than a few days
- A feeling that you need to have a bowel movement that's not relieved by having one
- Rectal bleeding with bright red blood
- Blood in the stool, which might make the stool look dark brown or black
- Cramping or abdominal (belly) pain
- Weakness and fatigue
- Unintended weight loss

Because colorectal cancers can bleed into the intestinal tract, signs of anemia may also be an early indicator of colorectal cancer. Signs of anemia:

- Fatigue
- Weakness
- Shortness of breath
- Lightheadedness

A rectal or abdominal mass is also a possible sign

The US Preventive Services Task Force recommends screening for all adults aged 50 to 75. Colorectal cancer screening strategies include stool tests, flexible sigmoidoscopy, colonoscopy, and CT colonography (virtual colonoscopy).

Those with an increased risk may need to be tested earlier than age 50 or more often than other people. Increased risk factors:

- You or a close relative have had colorectal polyps or colorectal cancer.
- You have an inflammatory bowel disease such as Crohn’s disease or ulcerative colitis.
- You have a genetic syndrome such as familial adenomatous polyposis (FAP) or hereditary non-polyposis colorectal cancer (Lynch syndrome).

Also see the QCancer®(15yr,colorectal) risk calculator.

Integrative Care in Colorectal Cancer

Before investigating integrative care in colorectal cancer, we recommend reviewing integrative cancer care in general.

Our goal is to help you live as well as you can for as long as you can. We provide information about using an optimal integrative combination of conventional and complementary therapies and approaches. In this handbook, we present a wide range of complementary therapies that have been studied for their effectiveness in colorectal cancer.

We give a brief description of what's known about these therapies. We also group natural products and off-label and novel therapies (which we call ONCAs) according to safety, effectiveness and ease of access.

We consider the cancer within the context of the whole person. Cancers are composed of cells that divide without stopping. Some divide slowly, others quickly. Some are more invasive than others. But they don't act independently of everything going on in your body.

Your body terrain—the internal environment that is influenced by external factors such as the foods you eat, the chemicals you contact, light and radiation you're exposed to, plus internal factors such as stress hormones, sex hormones, your fitness, feelings of being loved and your sense of purpose—can set the stage for whether cancer will grow and thrive. Will the cancer find the chemical and biological terrain that promotes growth or not? You have more control over this than you may realize.

Your body terrain can influence the tumor microenvironment—the biochemical and physical interaction of cancerous and noncancerous cells. The microenvironment makes the cancer either more or less likely to grow and spread. (See Body Terrain and the Tumor Microenvironment.) You may be able to improve your body terrain with an integrative approach.

A 2018 article in The Journal of Alternative and Complementary Medicine provides an excellent overview of integrative therapies: Integrative treatment for colorectal cancer: a comprehensive approach.9

Healing and Curing

Many of the integrative approaches in this handbook promote healing, which is not the same as curing. Healing is an inner process through which a person becomes whole. Healing can take

place at physical, emotional, mental and spiritual levels. An example of physical healing is when a surgical incision heals.

A cure is a successful medical treatment that removes all evidence of disease and allows the person who previously had cancer to live as long as he or she would have lived without cancer. For any cure to work, your healing power must be sufficient to enable recovery. Healing goes beyond curing and may happen whether or not the cancer is cured. Although the capacity to heal physically is necessary to any successful cure, healing can also take place on deeper levels, whether or not physical recovery occurs.

Whether or not your colorectal cancer is curable, healing is always possible and may provide these benefits:

- Slow the cancer's growth and spread
- Improve survival
- Reduce the risk of recurrence
- Alleviate symptoms and side effects
- Improve your overall well-being

Healing will help you feel whole regardless of how cancer may change your body or your life.

Use the information you find here to guide your choices in healing. Share this information with your cancer care team. We provide the evidence to date behind the therapies, and we group natural products and ONCAs—off-label, overlooked and novel cancer approaches—by their safety and strength of evidence to make it easier for your team to discern the best options for you and your specific situation.
Learn More

We recommend these resources to introduce you to conventional therapies and the science behind them:

- National Cancer Institute:
    - About Cancer
    - Colorectal Cancer—Patient Version
    - Colorectal Cancer—Health Professional Version
- Cancer.net: Colorectal Cancer

Knowing how your cancer behaves will influence the type of testing and treatment used, prepare you for possible treatment side effects and guide you in steps to prevent or minimize these effects. It will help you understand and choose the complementary therapies and lifestyle

approaches that may enhance your conventional treatment, manage side effects and improve your quality of your life.

You can also prepare your home team for what to expect. You can plan ahead to line up the support you may need. You can anticipate side effects and work to minimize them even before treatment starts. Finally, learning what to expect allows you to prepare mentally and spiritually to catalyze your resilience for facing the weeks and months to come.

You may read “the five-year survival for this cancer is X percent.” That means that this percentage of people survive at least five years. But expected survival doesn’t show the range of survival—which can vary from months to decades. We know many people who have lived far beyond the expectation. Getting healthier with cancer—and skillful use of conventional and complementary therapies—may help extend your life. It will very likely improve the quality of your life. There is nothing wrong with hope.

Clinical Practice Guidelines

- National Comprehensive Cancer Network:
    - Professional Guidelines (Login required):
        - Colon Cancer
        - Rectal Cancer
    - Guidelines for Patients:
        - Colon Cancer
        - Rectal Cancer

  American Society of Clinical Oncology: Gastrointestinal Cancer

Screening Guidelines

- Clinical Guidelines Committee of the American College of Physicians: Screening for Colorectal Cancer in Asymptomatic Average-Risk Adults: A Guidance Statement From the American College of Physicians (2019)
- British Medical Journal: Colorectal cancer screening with faecal immunochemical testing, sigmoidoscopy or colonoscopy: a clinical practice guideline (2019)
- The American College of Gastroenterology: ACG Clinical Guidelines: Colorectal Cancer Screening 2021

Guidelines following Curative Treatment

- Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons: Practice guideline for the surveillance of patients after curative treatment of colon and rectal cancer

Other Professional Recommendations

The US Preventive Services Task Force recommends initiating low-dose (81 mg) aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer in adults aged 50 to 59 years who have a 10 percent or greater 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.11 Use is not recommended for others, as risks from taking aspirin may outweigh benefits. Even those not at risk may experience catastrophic gastrointestinal bleeding.

Examples of Integrative Approaches

Bastyr Integrative Oncology Research Center (BIORC)

Between 2009 and 2014, 704 cancer patients were enrolled in an observational study at Bastyr Integrative Oncology Research Center (BIORC). Cancer types included lung, breast, ovarian, colon, pancreatic, brain and skin cancers. One-third of those patients had advanced cancer. BIORC used intravenous (IV) high-dose vitamin C, IV artesunate, oral curcumin, green tea and turkey tail mushrooms (Trametes versicolor).12

Preliminary results reported in 2013 from the BIORC are promising, as reported by BIORC's medical director and BCCT advisor Leanna J. Standish, PhD, ND, LAc, FABNO: “For eight patients with stage 4 colon cancer, BIORC reported an 80 percent survival rate after three years, compared with 15 percent from a group at Seattle Cancer Care Alliance.”13

> "Our patients are doing better than national averages," says Dr. Standish, a professor at Bastyr University and the University of Washington. "We don't know why. Maybe they would have done better, or maybe there's something about our treatment."

Similarly, of 12 BIORC patients with stage 4 lung cancer, 64 percent were alive after three years, compared with 15 percent from Seattle Cancer Care and three percent from a national data group. Limitations in most data sets make exact comparisons difficult.

Life Over Cancer System

The Block Center for Integrative Cancer Treatment (BCICT), founded by integrative oncologist and BCCT advisor Keith Block, MD, offers a comprehensive cancer treatment program combining

conventional treatments—often delivered in novel ways, such as according to circadian rhythms—along with nutrition and supplementation, fitness and mind-spirit instruction. The program is highly individualized and provides care to people with any kind of cancer.

Dr. Keith Block reported a case study of a 49-year-old man with colorectal cancer diagnosed in December 2002. Three years post diagnosis, after two surgeries and 12 chemotherapy cycles, he was in remission. In January 2006, he was diagnosed with stage 4 metastases.

Dr. Block prescribed an individualized program to enhance treatment tolerability, reduce treatment toxicity and boost treatment effectiveness through molecular profile testing. The Life Over Cancer program includes these therapies:

- Therapeutic nutrition to boost stamina, counter fatigue and reduce chemotherapy side effects
- Mind-spirit interventions to reduce stress
- Exercise to build strength and fitness
- Chronomodulated chemotherapy via a portable pump which deliversboth chemotherapy drugs and intravenous supplemental nutrients

The patient's outcome:

- He was able to stay active because of the portable pump.
- His scans improved.
- He reported no troubling side effects, and he tolerated the chemotherapy so well he did not need to reduce the dose.
- After seven chronotherapy sessions (five fewer than would have been used conventionally), he showed no evidence of disease (NED).
- As of the writing in 2009, seven years after his original diagnosis and three years after diagnosis of stage 4 metastases, the patient was in complete remission and back at work.
- For comparison, in the USA, colon cancer has a five-year life relative survival rate of 63 percent across all stages, and a 14 percent rate for distant spread (metastases).14

This approach is discussed in detail in a 2018 article, including Block’s use of three spheres of intervention: improving lifestyle, regulating biology, and enhancing treatment.15

The Ultimate Guide to Cancer: DIY Research

This guide from Ralph Moss, PhD, BCCT advisor and leading chronicler of integrative cancer treatments, shows you how to use four of the main tools that doctors use to decide on the best cancer treatments. It will help you learn why some cancer treatments that look good in clinical

trials may not work for “real world” patients. It will help you answer key questions that the doctor may be hesitant to answer in the detail you need to decide about treatment:

- What are my chances of actually living longer if I take your treatment?
- What are the likely side effects, and how long will they last?
- What other treatment options are available?

Also see The Moss Reports for comprehensive guidance on treating colorectal cancer.

Integrative Programs, Protocols and Medical Systems

Programs and protocols

- Alschuler & Gazella complementary approaches[16]
- Block program[17]
- Cohen & Jefferies Mix of Six anticancer practices[18]
- Lemole, Mehta & McKee colorectal cancer protocol[19]
- McKinney colorectal cancer protocol[20]
- Parmar & Kazcor treatment plans[21]
- Ayurveda
- Traditional Chinese medicine[22]
- Traditional Korean medicine[23]

Traditional Medicine Therapies

Throughout this summary, you will find examples of therapies used by, and in many cases created by, traditional medical systems. Foods and herbs such as medicinal mushrooms, soy and curcumin are part of traditional systems.

Evidence shows that herbs used in traditional Chinese medicine (TCM) may help in maintaining immune function in women with ovarian cancer, for comparison. Mind-body practices such as mindfulness meditation and yoga also have roots in these systems.

Acupuncture and electroacupuncture, another approach that is part of the Chinese and Korean medicine traditions, is used to relieve many symptoms during and following treatment. Electroacupunture even improved recovery of gastrointestinal function following surgery for colorectal cancer. See details below in Managing Side Effects and Promoting Wellness.

Integrative Therapies in Colorectal Cancer

7 Healing Practices: The Foundation

Top 5 Lifestyle Interventions following Colorectal Cancer Treatment

The authors of After Cancer Care: The Definitive Self-Care Guide to Getting and Staying Well for Patients with Cancer recommend these lifestyle interventions,24 which we've matched to the 7 Healing Practices:

- Be physically active every day. Even light intensity exercise has benefit (Moving More)
- Limit alcohol intake and do not smoke.(contributions from Managing Stress and Sharing Love and Support)
- Reduce animal-based and high glycemic index foods. (Eating Well)
- Emphasize plant-based whole foods rich in micronutrients, omega-3 fatty acids, fiber and calcium. (Eating Well)
- Maintain a healthy weight. (Eating Well and Moving More, with contributions from Managing Stress, Sleeping Well, and Sharing Love and Support)

Any of the 7 Healing Practices are a good beginning. Eating Well and Moving More pack a powerful one-two punch in potentially improving treatment outcomes, enhancing quality of life and/or reducing risk of recurrence in colorectal cancer. Moreover, evidence shows that Managing Stress, Sleeping Well, Creating a Healing Environment, Sharing Love and Support and Exploring What Matters Now can help patients and survivors. Ultimately, let your intuition guide you in choosing where to start with these healing practices.

Bundling Practices Leads to Better Results

People who followed the World Cancer Research Fund/American Institute of Cancer Research recommendations on diet, physical activity, and body fatness prior to a diagnosis of colorectal cancer showed better overall and cancer-specific survival after diagnosis. The more recommendations that were followed, the better the outcomes.25

A 2018 study of almost 1000 colorectal cancer survivors found a 42 percent reduction in death at five years for those who followed the American Cancer Society nutrition and physical activity guidelines most closely, compared to those who followed them least.26

Eating Well

Treating the Cancer

Some food choices are associated with better or worse survival:
Higher Survival

- Plant-rich, low-carbohydrate diet in patients with nonmetastatic colorectal cancer28

- Diet rich in omega-3 fatty acids29

Lower Survival

- High dietary insulin load30
- Red and processed meat[a]31

a. The association is for colon cancer only; no association was found between processed meat intake and overall survival or disease-free survival for rectal cancer.32

Flax seeds, garlic, green tea and mushrooms and are among the plant foods most commonly used by oncology naturopaths for colorectal cancer.33

An observational study of patients with stage 3 colon cancer treated with surgery and adjuvant chemotherapy found a link between eating two or more weekly servings of tree nuts and improved disease-free survival and overall survival compared to no nut consumption.34

The ability of foods to influence inflammation may also impact survival. A diet with more anti-inflammatory potential improved overall survival among postmenopausal women diagnosed with colorectal cancer.35 Foods and food components with anti-inflammatory properties:

Beta-carotene
B vitamins (several of the individual vitamins)
Caffeine
Eugenol
Fiber
Folic acid
Garlic
Ginger
Isoflavones and other phytonutrients
Magnesium
Mono- and polyunsaturated fatty acids
Onions
Oregano
Rosemary
Selenium
Saffron
Tea
Thyme
Turmeric
Vitamin A
Vitamin C
Vitamin D

Vitamin E
Zinc

Managing Side Effects and Promoting Wellness

Higher intake of dietary magnesium is associated with less prevalent and less severe chemotherapy-induced peripheral neuropathy in colorectal cancer patients.36 Foods high in magnesium include these:37

Almonds
Black beans
Cashews
Dark chocolate
Edamame beans
Peanuts
Pumpkin seeds
Soy milk
Spinach
Whole-wheat bread or shredded wheat cereal

The Cancer.Net Editorial Board of the American Society of Clinical Oncology recommends a balanced diet that includes specific nutrients such as B vitamins (including B1 and B12, folic acid) and antioxidants (see Antioxidants and Cancer Outcomes below) to reduce pain from peripheral neuropathy. They also recommend reducing alcohol consumption.38

These foods are among those rich in B vitamins:39

Eggs
Leafy Greens
Liver and Other Organ Meats
Milk
Salmon

Commentary: Eggs and Cancer

Integrative naturopathic oncologist and BCCT advisor Lise Alschuler, ND, FABNO, and her colleague Karolyn Gazella advise people with risk for colon cancer to consider limiting egg intake to fewer than five eggs a week, while choosing eggs from free-roaming, organically fed chickens. They also advise boiling or poaching eggs, as these methods do not oxidize the yolk fat.805

Inflammation and Side Effects

As integrative oncologist and BCCT advisor Keith Block, MD, explains: Inflammation can bring on cachexia—the severe wasting syndrome common among patients with solid tumors—and,

especially, metastases. Cachexia, which is particularly common in cancers of the pancreas, colon and lung, can lead to the rapid breakdown of muscle, including the heart muscle.342

Inflammation is associated with cachexia,343 as inflammatory cytokines cause reduced appetite and abnormal metabolism of proteins, fats and carbohydrates. All this leads to loss of muscle and weight.344

Reducing Risk

Western dietary patterns—such as eating large amounts of processed meats and refined grains and low quantities of vegetables and fruits—has been associated with higher risk of tumor recurrence and mortality in colorectal cancer.40 More than 52,000 new colorectal cancer cases in the United States in 2015 were estimated to be associated with suboptimal diet among US adults.41 The American Institute for Cancer Research recommends a plant-based diet with a variety of fruits, vegetables, beans and whole grains to lower risk.42

As mentioned above, the Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons recommends a balanced diet after curative treatment of colon and rectal cancer.43 One such balanced diet—the Mediterranean diet, and specifically its components olive oil, red wine, and tomatoes—is associated with clinically reduced cancer initiation and progression.44

Strong evidence shows these associations between food choices and risk of colorectal cancer or recurrence:
Lower Risk, from many sources45

- Whole-grain foods
- Dietary fiber, found in whole grains, many fruits and vegetables, and legumes such as black beans, chickpeas or lentils[a]
- Dairy foods, such as milk and plain yogurt
- Foods rich in marine omega-3 fatty acids, such as fish and fish oils[b]
- Foods high in calcium, such as dairy foods and dark green leafy vegetables

Higher Risk, from many sources46

- Processed meat (preserved by curing, salting, smoking, drying or canning)
- Red meat
- Alcohol

a. Some evidence shows that fiber's benefit may involve the gut microbiome.47
b. Some evidence of reduced risk in men but not women48

A large study concluded that a moderate reduction in fat consumption did not reduce the risk of invasive colorectal cancer in postmenopausal women during more than eight years of follow-up.49

Studies and expert assessments have further concluded that these foods and dietary choices may also lower risk of developing colorectal cancer or recurrence of adenomas:50

- Foods containing vitamin C, found in peppers, parsley, kale, kiwis, broccoli, Brussels sprouts, lemons, strawberries, oranges and other foods
- Fish
- Non-starchy vegetables such as dark green and leafy vegetables
- Fruit
- Foods rich in folate (Healthline), such as legumes (lentils, peas and dried beans), asparagus, eggs, leafy greens and other foods
- Poultry, fish or legumes (dried beans, lentils and peas) instead of red meat
- Food with anti-inflammatory components (see the list above), including flavonols (such as quercetin) and vitamin D

Although early investigations suggested a protective effect of high intake of raw and/or cooked garlic against colorectal cancer,51 more recent analyses show no protective effect.52

Researchers evaluating the evidence across 80 meta-analyses of interventional and observational studies of colorectal cancer prevention found no evidence of a protective effect for tea, coffee, fish and soy products.53

Evidence shows that these foods may increase risk of colorectal cancer:

- Foods containing heme iron (red meat, chicken and fish) might increase the risk of colorectal cancer.54
- Foods with a high dietary inflammatory index:55
- Red and processed meats
- Refined carbohydrates
- Fried foods
- Sugar-sweetened beverages
- Margarine, shortening and lard

Antioxidants

Prospective randomized trials have not shown that antioxidant supplements prevent colorectal adenoma or carcinomas.56

B Vitamins

Higher dietary intakes of folate and riboflavin (vitamin B2) are associated with decreased risk.57 Eating foods higher in vitamin B12 was also associated with lower risk.58 and with an overall low-risk diet and lifestyle in a population at high risk for colorectal cancer.59 Good sources of these nutrients:60

Folate

- Broccoli
- Brussels sprouts
- Leafy green vegetables (cabbage, kale, spring greens and spinach)
- Peas
- Legumes such as chickpeas and kidney beans

Riboflavin

- Eggs[a]
- Fortified breakfast cereals
- Milk
- Mushrooms
- Plain yogurt

Vitamin B12

- Fish
- Milk
- Cheese
- Eggs
- Fortified breakfast cereals

a. See recommendations about eggs in the Commentary section below.

Unlike the B vitamins listed above, dietary intake of vitamin B6 shows mixed results:

- Reducing risk of colorectal cancer in some studies61
- Higher serum levels of vitamin B6 was associated with reduced risk in 50- to 69-year-old men.62
- A large meta-analysis found a slight decrease in colorectal cancer risk associated with the higher level of vitamin B6 intake. This decrease was not statistically significant, and dietary intake was not separated from supplement use.63
- Dietary B6 intake greatly increased risk of rectal cancer in women in one study.64
- A large study of US women aged 45 years or more found that dietary intakes of folate and vitamin B6 were associated with lower colorectal cancer risk only among women who were not taking supplements containing folate and vitamin B6.65

The takeaway with vitamin B6 is that its impact on colorectal cancer risk is uncertain. Benefits may apply only to specific groups or specific cancer types. To date, no compelling evidence suggests that the presence of vitamin B6 should be a priority in your dietary choices.

Calcium and Magnesium

- Higher intake of calcium in drinking water reduces risk of incidence and death from colon cancer.66
- Higher intake of dietary magnesium reduces risk of colorectal cancer, especially colon cancer.67
- With higher intake of magnesium or higher calcium-to-magnesium ratios, risk is also reduced for colorectal adenoma, but only in people with specific genes (genotypes).68

Fiber

Fiber feeds the friendly bacteria in your gut, and so is considered a prebiotic. Fiber is fermented by intestinal microorganisms into short-chain fatty acids, the most abundant of which is butyrate. Butyrate is necessary for normal metabolism but is not derived directly from food—it has to be created by bacteria fermenting fiber. Patients with colorectal cancer tend to have lower levels of butyrate-producing bacteria than other people.

Butyrate may be a reason that fiber is connected to colorectal cancer prevention. Butyrate is selectively transported into the lining of the colon, where it is used by normal colon cells for much of their energy needs. However, in cancer cells it accumulates in parts of the cell where its action is to suppress cell growth, induce cell death (apoptosis) and promote differentiation. In cell studies, butyrate inhibits colorectal cancer cell growth.69

Optimizing Your Terrain

Beneficial Foods

- Butyrate (from fiber, see above) is a potent anti-inflammatory. It lessens inflammation related to colitis in both rodents and humans.70
- Green tea consumption decreased fasting glucose and glycated hemoglobin (HbA1c) concentrations.71
- Cocoa is antioxidative and anti-inflammatory72

Foods to Avoid

Diets high in cholesterol (WebMD) are linked to increased inflammation.73

Ask for Guidance

A small study of colorectal cancer survivors in the United Kingdom found that most—more than 2/3—reported receiving no nutritional advice from their doctors and care teams.27 We have no reason to believe the situation is much better anywhere else.

If your team doesn't provide guidance, ask your doctor for a referral to a dietician or nutritionist who specializes in counseling cancer patients and survivors. Even better, seek out an integrative healthcare provider (medical doctor, osteopathic doctor, naturopath, nurse or physician assistant who practices an integrative approach) if you'd like specific guidance about what to eat to improve your outcomes and manage side effects.

Moving More

Treating the Cancer

Participating in regular physical activity reduces mortality:

- Reduced risk of colorectal cancer-specific mortality or overall mortality with any physical activity, with even lower risk with high levels of physical activity after diagnosis74
- People diagnosed with colorectal cancer who are at high levels of fitness had an 89 percent decreased risk of all-cause mortality75
- Each 15 MET-hours (metabolic equivalent task-hours) per week increase in physical activity after colorectal cancer diagnosis was associated with a 35 percent lower risk of colorectal cancer–specific mortality.76 Fifteen MET-hours per week is represented by any one of these activities:77
    - 5 hours of general housecleaning, or
    - 3½-4 hours of very brisk walking (4 miles per hour), or
    - 3½-4 hours of moderate bicycling (10 to 12 miles per hour), or
    - 2 to 2½ hours of singles tennis

Managing Side Effects and Promoting Wellness

Physical activity benefits some side effects and overall quality of life:

Quality of Life

- Survivors who met recommendations for physical activity reported higher health-related quality of life compared to those not meeting recommendations.78
- Physical activity directly related to improved physical function in older, long-term colorectal cancer survivors.79
- Physical activity was associated with higher total quality of life score, physical well-being, functional well-being, and other measures of quality of life.80
- Colorectal cancer survivors meeting Canadian public health exercise guidelines reported clinically and significantly better quality of life.81

- An exercise intervention among recently surgically resected colorectal cancer survivors found improved quality of life.82
- Previously active individuals who fail to reinitiate exercise after cancer treatment experience the lowest quality of life one to four years later compared to those who maintain activity, temporary relapsers and nonexercisers.83

Fatigue

- Colorectal cancer survivors meeting Canadian public health exercise guidelines reported clinically and significantly reduced fatigue.84
- Physical exercise has a positive effect on fatigue among cancer patients.85

Nausea

- Physical exercise has a positive effect on nausea.86

Sleep Disturbance

- While evidence shows that physical activity does promote better sleep87 sleep disturbance among colorectal cancer patients coming off first-line treatment was not improved by either an increase in exercise or a level of physical activity at or above American College of Sports Medicine's guidelines.88

Reducing Risk

The Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons recommends regular exercise after curative treatment of colon and rectal cancer.89

Strong evidence shows that being physically active decreases the risk of colon cancer. Evidence is not conclusive regarding rectal cancer.90

- Those with high fitness showed a substantially decreased risk of incident colorectal cancer.91
- A large 2019 analysis found that engaging in 7.5 to 15 MET-hours per week (about 2.25 to 4.5 hours of brisk walking) was associated with a lower risk of colon cancer in men, as well as other types of cancer.92

Managing Stress

Reducing Risk

Higher perceived stress is associated with increased risk of rectal cancer, but not colon cancer.93

Sleeping Well

Treating the Cancer

Sleep duration and timing may impact survival:

- Short sleep duration (less than 5 hours per night) before diagnosis was associated with a 36 percent higher risk of all-cause mortality and a 54 percent increase in colorectal cancer mortality among colorectal cancer survivors.94
- Napping one hour or more per day before diagnosis was associated with significantly higher total and cardiovascular disease mortality but not colorectal cancer mortality.95 Colorectal cancer patients sleeping two or more hours during the day had a significantly increased risk of all-cause mortality compared to individuals with no daytime sleep.96 Keep in mind, however, that this does not mean that napping caused greater mortality. It's very possible that those who were already sicker needed to nap more, or that napping indicated disturbed nighttime sleep, and these underlying conditions contributed to greater mortality.

Circadian disruption—activity during sleeping hours and a lack of restful sleep—during chronomodulated chemotherapy is associated with shorter overall survival:

- The rest/activity rhythm was a strong predictor of both tumor response and survival in patients with metastatic colorectal cancer: patients with the poorest circadian rhythms had a five-fold higher risk of dying within two years than the patients with better circadian rhythms.97
- Patients with a disturbed circadian rhythm survived an average of 14.7 months compared to 22.3 months for patients with a robust circadian rhythm.98
- If a patient's circadian rhythms are disrupted by chemotherapy, chronomodulated therapy may not be as effective. Chemotherapy-induced fatigue and weight loss—both of which are related to poor sleep quality—early in therapy may impair the benefits of chonomodulated therapy on survival and time to progression.99 The researchers suggest monitoring patients to detect early chemotherapy-induced circadian disruption. This will allow for adjustments in chronotherapy to improve safety and effectiveness.

Managing Side Effects and Promoting Wellness

Patients with restful sleep, as measured by clear distinctions between period of rest and of activity, had better quality of life and reported significantly less fatigue than patients with disrupted sleep. Disrupted circadian rhythms led to worse chemotherapy-related symptoms as well as patients' perception of them.100

Sleep disturbance was associated with anxiety and fatigue among colorectal cancer survivors.101

Reducing Risk

The Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons recommends regular sleep after curative treatment of colon and rectal cancer.102

- A 2014 review concluded that maintaining a regular and adequate daily amount of sleep reduces risk of colorectal cancer.103 However, long sleep duration—sleeping nine or more hours per night—is associated with an increased risk of colorectal cancer (but does not necessarily cause increased risk).104
- An extensive meta-analysis did not find an overall association between ever-exposure to night-shift work and the risk of colorectal cancer.105

Improving Sleep

Interventions recommended by integrative oncologist and BCCT advisor Dr. Keith Block to improve circadian rhythms and sleep for cancer patients:106

- Develop routine sleep habits.
- Get exposure to early morning bright light.
- Dispel incorrect notions about sleep.
- Keep your bedroom cool and dark.
- Supplement with melatonin.
- Consider cognitive-behavioral therapy for insomnia, which is effective for sleep problems in most cancers.

Creating a Healing Environment

Reducing Risk

Several environmental exposures are associated with increased risk of colorectal cancer:107

- 1,1-dichloroethane used in industrial manufacturing of other chemicals, as a solvent for cleaning and degreasing, and in the manufacture of plastic wrap, adhesives, and synthetic fiber
- Alachlor, an herbicide
- Aromatic amines
- Chlorination byproducts
- Ionizing radiation
- Nitrates in water
- Solvents

Chemicals formed during food processing—nitrosamines, heterocyclic amines and polycyclic aromatic hydrocarbons—may also be related to increased risk of colorectal cancer.108

Sharing Love and Support

Managing Side Effects and Promoting Wellness

In a systematic review, emotional support and reassurance when trying to deal with fear of cancer recurrence featured as the most prominent supportive care need of colorectal cancer patients, regardless of clinical stage or phase of treatment.109

Evidence of the impact of social support on quality of life and symptoms:

- Lower levels of social support were correlated with higher levels of psychological distress among middle-aged colorectal cancer patients and their healthy spouses.110
- In patients undergoing surgery for colorectal cancer, greater social support, as well as improvements in insomnia and in physical, cognitive, and social functioning, improved anxiety and depression 12 months after surgery.111
- Greater perceived social support and resilience was associated with greater posttraumatic growth (positive change experienced as a result of the struggle with a major life crisis or a traumatic event) in colorectal cancer survivors with permanent intestinal ostomies.112
- Poorer quality of life outcomes (generic health-related quality of life, reduced well-being, anxiety, and depression) were significantly associated with lower levels of social support up to two years after surgery to cure colorectal cancer.113

Clinicians are encouraged to be “aware of situations that might necessitate intervention of other professionals, either medical or pastoral. Attention to psychosocial events is an integral part of a comprehensive oncologic program to facilitate patients and families to live in an atmosphere of peace and dignity.”114

Reducing Risk

Greater social support is related to greater engagement with colorectal cancer screening among Americans of African descent. Social support is also related to informed decision making about colorectal cancer screening among African American men in particular.115

Exploring What Matters Now

Managing Side Effects and Promoting Wellness

Making sense of the cancer experience was identified as a core theme affecting quality of life issues for colorectal cancer patients.116

Beyond the 7 Healing Practices: Further Integrative Therapies

Conventional treatments are readily available. Complementary therapies can be useful to enhance conventional treatment effects, improve quality of life and possibly even extend life for those with colorectal cancer. Many complementary therapies—when chosen thoughtfully, reviewed with your oncology treatment team and used alongside conventional therapies—can become part of your integrative cancer care approach.

Therapies are grouped according to their effects:

- Treating the cancer
- Managing side effects and promoting wellness
- Reducing risk
- Optimizing Your Terrain

We present natural products in six groups:

1. Good clinical evidence of efficacy & safety, easy access
2. Good clinical evidence of efficacy & safety, limited access
3. Limited clinical evidence of efficacy but good safety, used in leading integrative programs
4. Limited clinical evidence of efficacy, or significant cautions, but potential significant benefit
5. Especially promising preclinical or emerging clinical evidence of efficacy and safety
6. Evidence of no efficacy or may be dangerous

Off-label, overlooked and novel cancer approaches (ONCAs) are grouped separately:

Group A: Good clinical evidence of efficacy
Group B: Limited clinical evidence of efficacy
Group C: Promising preclinical evidence only
Group D: Evidence of no efficacy or may be dangerous

Within each section, we list only groups containing applicable therapies.

Other integrative therapies and approaches are described but not categorized. See the full summaries as linked for more information on each of these therapies.

Treating the Cancer

Working against cancer growth or spread, improving survival, or working with other treatments or therapies to improve their anticancer action

Conventional Treatments

Conventional treatments for colorectal cancer include these:

- Surgery (also see Surgery and Colorectal Cancer below)

- Radiofrequency ablation
- Cryosurgery
- Chemotherapy
- Radiation therapy
- Targeted therapy
- Immunotherapy

These treatments are explained on the National Cancer Institute website: Colorectal Cancer—Patient Version and Colorectal Cancer—Health Professional Version.

Newer conventional treatments and outcomes:

- Pressurized intraperitoneal aerosol chemotherapy (PIPAC) is a relatively new treatment for patients with peritoneal metastases. A 2019 review found an objective clinical response of 71–86 percent for colorectal cancer (median survival of 16 months) with PIPAC. Repeated PIPAC did not have a negative effect on quality of life.118
- Pulsed low-dose rate radiation therapy (PLDR-RT) delivers conventional radiation doses in pulses of small doses with intermittent pauses. A small study involved PLDR-RT for patients with rectal and other cancers of the pelvis. Patients had undergone radiation therapy to the pelvis previously. Twenty-three patients were treated with a curative intent and 15 were treated palliatively. At one year, 59 percent of patients treated for curative intent had a clinical, biochemical or radiographic response, and six of the 23 patients had no evidence of disease at their last follow-up. Among the patients treated palliatively, 61 percent had a clinical or radiographic response.119 This delivery also produces low rates of toxicity, along with reduced damage to noncancerous tissue and decreased repair of DNA damage in tumor cells.

Conventional treatments can be very expensive, and some treatments can cause long-lasting side effects.120 We encourage you to explore the benefits, risks and costs of all options.

Avoiding Drug Interactions during Treatment

Potentially life-threatening interactions between drugs are possible. For example, proton pump inhibitors (PPIs) can increase the risk for progression in colorectal cancer patients being treated with adjuvant CAPOX (capecitabine with oxaliplatin) or FOLFOX (leucovorin calcium [folinic acid], fluorouracil, and oxaliplatin). PPIs have a significant effect on both progression-free and overall survival.

Experts conclude that “it is better to avoid PPIs during chemotherapy for colorectal and gastrointestinal tumors,” and avoid polypharmacy (the simultaneous use of multiple drugs to treat a single ailment or condition) whenever possible.

From a report on a keynote speech from the ESMO 22nd World Congress on Gastrointestinal Cancer Virtual Experience in 2020.117

Delaying Treatment

Some providers offer a “watch-and-wait” approach for select rectal cancer patients who have had a clinical complete response after neoadjuvant therapy. While this approach has resulted in excellent rectal preservation and pelvic tumor control, a 2019 study found it has also resulted in worse survival and a higher incidence of distant progression in patients with local regrowth compared to those without local regrowth.121 A review and meta-analysis in late 2020 confirmed that delaying colorectal cancer treatment by a month or more increases the risk of dying.122

Factors Influencing the Success of Treatment

Characteristics of both healthcare providers and the patient can impact the likelihood of success in treatment.

A surgeon’s or hospital’s frequency of performing high-risk surgeries can influence treatment outcomes. Surgeons and hospitals that do not perform at least a minimum number of these surgeries every year have a higher likelihood of errors, complications and even death. A 2019 review concluded that the minimum number of rectal cancer surgeries for competence was 16 for a hospital and six for each surgeon.123

Outcomes from all therapies and treatments can be influenced by a patient’s physical and psychosocial situation.124

- Co-existing (comorbid) conditions such as diabetes, high blood pressure, heart disease, asthma and many more can impact a patient’s response to demanding therapies such as surgery and chemotherapy.
- Psychosocial risk factors such as a lack of resourcefulness, depression, alcohol abuse, or the absence of social support can also influence the completion and success of many treatments.

More on Conventional Treatments

We recommend these resources to introduce you to the science of colorectal cancer and conventional therapies:

- National Cancer Institute:

    - About Cancer
    - Colorectal Cancer—Patient Version
    - Colorectal Cancer—Health Professional Version
- Cancer.net: Colorectal Cancer

Natural Products

Antioxidants and Cancer Outcomes

Substances that act as antioxidants can have both antitumor and tumor-promoting effects, depending on several factors:125

- The specific antioxidant, plus the dose and format used
- Characteristics of the patient: poor nutrition, smoking or high alcohol intakes may cause antioxidants to act as pro-oxidants and promote cancer growth
- The tumor site and therapy: antioxidants can act as pro-oxidants in tissues with elevated partial pressures of oxygen.

Many substances can serve as antioxidants and are abundant in these food sources:

- Allium sulphur compounds in leeks, onions and garlic
- Anthocyanins in eggplant, grapes and berries
- Beta-carotene in pumpkin, mangoes, apricots, carrots, spinach and parsley
- Catechins in red wine, tea leaves (especially green tea), cocoa and berries
- Copper in seafood, lean meat, milk and nuts
- Coumaric acid in spices and berries
- Cryptoxanthin in red bell peppers, pumpkin and mangoes
- Flavonoids, particularly flavonols in tea leaves (especially green tea), citrus fruits, red wine, onions and apples
- Indoles in broccoli, cabbage and cauliflower and other cruciferous vegetables
- Isoflavonoids in soybeans, tofu, lentils, peas and milk
- Lignans in sesame seeds, bran, whole grains and vegetables
- Lutein in corn and green, leafy vegetables such as spinach
- Lycopene in tomatoes, pink grapefruit and watermelon
- Manganese in seafood, lean meat, milk and nuts
- Polyphenols in thyme and oregano
- Quercetin in apples, red wine and onions
- Resveratrol in red and white wine, grapes, peanuts and berries
- Selenium in Brazil nuts, seafood, animal organs, lean meat and whole grains
- Vitamin A in liver, sweet potatoes, carrots, milk and egg yolks
- Vitamin C in oranges, black currants, kiwifruit, mangoes, broccoli, spinach, bell peppers and strawberries
- Vitamin E in vegetable oils such as wheat germ oil, avocados, nuts, seeds and whole grains
- Zinc in seafood, lean meat, milk and nuts

- Zoochemicals in red meat, organ meats and fish

Many of these individual antioxidants are also available as dietary supplements.

Antioxidants have mixed effects on chemotherapy toxicity, but no trials have assessed long-term effects of antioxidant supplementation during chemotherapy on recurrence or survival.

Mixed effects of antioxidants have been seen in reducing toxicity of radiotherapy, although not involving colorectal cancer patients. Observational studies in colorectal cancer patients have found that those taking self-prescribed multivitamins showed neither benefit nor harm regarding toxicity or survival.126

Antioxidants may reduce chemotherapy and radiotherapy toxicity, but they also can make these treatments less effective. The anticancer effects of radiotherapy and certain chemotherapy drugs, including alkylating agents, anthracyclines, podophyllin derivatives, platinum complexes and camptothecins, may come from producing reactive oxygen species and increasing cell death. A 2014 review concluded that accumulating evidence "does not support the widespread use of antioxidants in patients with cancer."127

Antioxidants have shown little to no effect on reducing risk of colorectal cancer.128 Some evidence shows benefit in reducing recurrence: patients receiving an antioxidant compound of selenium, zinc, vitamin A, vitamin C and vitamin E were significantly less likely to have an adenoma recurrence.129

Use of tobacco and alcohol is an important consideration when considering antioxidant supplements. One analysis found that supplementation with antioxidants decreased the recurrence of colon adenomas among people who neither smoke nor drink alcohol, but use doubled the risk among participants who smoked and also drank more than one alcoholic drink per day.130

Evidence and cautions regarding eating foods rich in antioxidants are described in Eating Well above, while those related to supplements are listed in the Natural Products sections.

Group 1: Good clinical evidence of efficacy & safety, easy access

These therapies may be widely used in integrative cancer protocols and traditional medical systems.

Medicinal mushrooms

- Turkey tail mushrooms or extracts:

- PSK (an extract of turkey tail mushrooms) improved both survival and disease-free survival of patients with advanced stomach and colorectal cancer or with curatively resected colorectal cancer.131
- Improved survival in colorectal cancer.132
- Improved 5-year disease-free survival and reduced lung metastases when used with oral Tegafur/Uracil133
- Improved recurrence-free survival, cancer death survival, and overall survival rates when added to chemotherapy treatment, but only among patients with diffuse nuclear accumulation-type beta-catenin activation134
- Improved 10-year survival when added to oral treatment with fluoropyrimidines135
- Among the botanicals most commonly used by oncology naturopaths for colorectal cancer136
- Shiitake mushroom extracts
- Improved survival in patients with gastric or colorectal cancer137
- Other medicinal mushrooms with preclinical evidence only:138
- Chaga mushroom (Inonotus obliquus)
- Pearl oyster mushroom (Pleurotus ostreatus)
- Indian or lung oyster mushroom (Pleurotus pulmonarius)
- Used in these programs and protocols:
- Alschuler & Gazella complementary approaches139
- McKinney protocols140

Vitamin D

- Reduced mortality with higher serum levels141
- Increased five-year relapse-free survival in patients with digestive tract cancers who had baseline serum 25(OH)D levels between 20 and 40 ng/mL, but no improvement in five-year overall survival from vitamin D3 supplementation after surgery142
- Improved survival and progression-free survival in patients with advanced or metastatic colorectal cancer with high-dose vitamin D3 supplementation compared to standard-dose vitamin D3143

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Astragalus

- Limited evidence of increased tumor response rate and survival when used with chemotherapy to treat colorectal cancer144
- Noteworthy preclinical evidence:145
- Works against proliferation (antiproliferative)
- Works against invasion (anti-invasive)
- Promotes cell death (proapoptotic)
- Induces cell cycle arrest
- Prevents the development of new blood vessels (anti-angiogenic)

- Formononetin, an astragalus extract, reduced metastasis and tumor growth in animals and reduced cell invasion and blood vessel development (angiogenesis) with tolerable toxicity
- Used in the Block program146 in combination with several other natural products in conjunction with conventional treatment

Curcumin

- Decreased serum TNF-α level (a marker of inflammation), increased cell death (apoptosis), and enhanced expression of p53 (a tumor suppressor gene) in tumor tissue in patients with colorectal cancer after diagnosis and before surgery147
- Significant tumor marker response and some clinical benefit, although no antitumor activity in a small trial of liposomal curcumin in metastatic advanced cancer148
- Reduced a marker of inflammation in a meta-analysis (not specific to people with cancer)149
- Well tolerated and effective with FOLFOX (5-fluorouracil, oxaliplatin, and gemcitabine)150 with some evidence of improved survival151
- Notable preclinical evidence of effects:
    - Induced cell death (apoptosis) in colorectal cancer cells152 and several other modes of anticancer action153
    - Enhanced effects of the chemotherapy drug irinotecan on colorectal cancer cells154
    - Enhanced anticancer activity of the chemotherapeutic drug 5-fluorouracil155
    - Inhibited and reversed EMT (epithelial-to-mesenchymal transition), a process involved in tumor progression, invasion, migration and metastasis, plus reduced resistance to chemotherapy156
- Used in these programs and protocols:
    - Alschuler & Gazella complementary approaches157
    - Bastyr University Integrative Oncology Research Center
    - Lemole, Mehta & McKee protocols158
    - McKinney protocols159
- Among the botanicals most commonly used by oncology naturopaths for colorectal cancer160

Fermented wheat germ extract

- Improved response to chemotherapy and radiotherapy, extending both progression-free survival and overall survival, including in advanced stages161
- Notable preclinical effects:
- Interacted with 5-fluorouracil (5-FU) or dacarbazine (DTIC) in mouse models, reducing tumor size and metastasis162
- Promoted cell death (apoptosis) in cancer cells,163 including colon cancer cell lines164
- Reduced proliferation of cancer cells,165 including colon cancer cell lines166
- Used in these protocols and programs:

- Block program167
- Parmar & Kazcor treatment plans168

Green tea extracts/EGCG

The effects of drinking tea are discussed above in Eating Well.

- Inhibited tumor stem cell proliferation, prevented tumor production, and reduced risk of recurrence after surgery169
- Prevented the development and progression of precancerous lesions, such as colorectal adenomas,170 and reduced incidence of metachronous (not concurrent) adenomas after colorectal adenomas were removed171
- Notable preclinical evidence:
    - Protected animals from colon cancer induced by azoxymethane (a substance used in cancer research to cause colon tumors in laboratory animals)172
    - Inhibited polyp formation in animals and suppressed small intestinal tumor formation in mice173
    - Inhibited tumor incidence, with near-normal survival rate and restoration of normal colon architecture in rodents174
    - Inhibited precancerous polyps and development of colon cancer in mice fed a high-fat diet175
    - Inhibited development of intestinal, colon and stomach cancer176
- Used in these Programs and Protocols:
- Alschuler & Gazella complementary approaches177
- Block program178
- Lemole, Mehta & McKee protocols179

Melatonin

- Increased one-year survival rate and objective tumor regression rate in patients treated with melatonin and chemotherapy compared to those receiving chemotherapy alone (with several cancers including gastrointestinal tract neoplasms)180
- Increased one-year survival rate compared to supportive care alone or when combining subcutaneous low-dose interleukin-2 (a type of cytokine or immune protein that boosts the activity of certain immune cells) with melatonin181
- Increased disease control in patients with metastatic colorectal cancer when added to treatment with irinotecan182
- Used in these programs and protocols:
- Alschuler & Gazella complementary approaches183
- Block program184
- Lemole, Mehta & McKee protocols185
- McKinney protocols186
- Parmar & Kazcor treatment plans187

Mistletoe (European)

- Longer disease-free survival188
- Can be highly toxic if used inappropriately; see Cautions in the full review
- Used in the Parmar & Kazcor treatment plans189

Omega-3 fatty acid supplements

The effects of omega-3s in your diet are discussed above in Eating Well.

- Lower risk of colorectal cancer-specific mortality with higher intake (from both diet and supplements) after diagnosis190
- Reduced length of hospital stay, but no reduction in noninfectious complications or mortality when taken before surgery in a nutritional supplement also including arginine and nucleotides191
- No decrease in tumor size or improvement in patient survival times in a 2015 review192
- Increased cell death (apoptosis) in the normal sigmoid colon with a dietary decrease in omega-6s and increase in omega-3s for two years193
- Eicosapentaenoic acid (EPA) effects:
- Improved overall survival in patients undergoing liver resection surgery for colorectal cancer liver metastases194
- Reduced extent of blood vessel networks consistent with reduced creation of new blood vessels to supply tumors (angiogenesis) with EPA use195
- Reduced crypt cell proliferation and increased cell death (apoptosis) in people with colorectal adenomas with three months of supplementation196
- Used in these programs and protocols:
- Alschuler & Gazella complementary approaches197
- Block program198
- Lemole, Mehta & McKee protocols199
- McKinney protocols200
- Parmar & Kazcor treatment plans201

Resveratrol

- Increased markers of cell death (apoptosis) in cancerous liver tissue in patients with colorectal cancer and liver metastases202
- Reduced tumor cell proliferation by 5 percent in a small study203
- Notable preclinical effects:
- Prevented formation of colon tumors and reduced their numbers and reduced the formation of small intestinal tumors by 70 percent in mice204
- Sensitized colon cancer cells to 5-fluorouracil205
- Used in these programs and protocols:
- Block program206
- Lemole, Mehta & McKee protocols207
- McKinney protocols208

Group 4: Potential significant benefit, but either limited clinical evidence of efficacy or significant cautions

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Aged garlic extract

The effects of garlic in your diet are discussed above in Eating Well.

- Reduced size and number of colon adenomas in colorectal cancer patients209
- Caution regarding increased risk of colorectal cancer with use

Combinations of therapies

- Hedyotis, astragalus and scutellaria
    - Increased tumor response rates when used with oxaliplatin-based regimens in the palliative treatment of colorectal cancer210
- Kangai injection (KAI, ginseng, Astragali radix and kushen)
    - Increased clinical effectiveness and survival time with in advanced colorectal cancer patients receiving chemotherapy211
- LC09 (Astragalus membranaceus, flowers carthami, lithospermum, Geranium wilfordii, and Radix angelicae)
    - Increased chemotherapy completion rate in colorectal cancer patients with chemotherapy-associated hand-foot syndrome212
- MB-6, a combination of fermented soybean extract, green tea extract, Antrodia camphorata mycelia, spirulina, grape seed extract, and curcumin extract
    - Enhanced chemotherapy effects and outcomes:213
    - Reduced disease progression rate, incidence of adverse events (at least grade 4) and occurrence of increased serum creatinine (an indicator of kidney toxicity) in a small clinical study of patients with metastatic colorectal cancer when combined with leucovorin, 5-fluorouracil, and oxaliplatin compared to chemotherapy alone
    - Increased the survival rate and life span of mice bearing colon cancer tumors when combined with chemotherapy as compared with chemotherapy alone
- Paeonia, curcuma, and sophora
    - Increased tumor response rates when used with oxaliplatin-based regimens in the palliative treatment of colorectal cancer214
- Quxie Capsule, a combination of traditional Chinese medicine therapies
    - Increased median overall survival, but not progression-free survival, in some small studies215 but not all216
    - Noteworthy preclinical evidence:
    - Lower mean tumor weight in mice and increased cell death (apoptosis)217

L-carnosine

- Promoted cell death (apoptosis) when used with FOLFOX-6 regimen218

Vitamin B3 supplements

- Increased 5-FU delivery to colorectal cancer liver metastases, but did not increase 5-FU retention or tissue exposure219

Vitamin C supplementation or intravenous use

- Associated with tumor regression in advanced colon cancer and improved toleration of standard therapy220
- Improved survival in patients with many cancer types221
- Notable preclinical evidence:222
    - High levels (with intravenous use) selectively kill colorectal cancer cells and impair their growth in mice
    - Overcame chemoresistance to cetuximab in mutated colorectal cancer cells

Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Arabinogalactan

- Decreased tumor size and weight in mice, plus other anticancer activity223
- Reduced liver metastases and prolonged survival of animals when administered with D-galactose224

Grape seed extract

- Inhibited lung metastasis in mice225
- Inhibited cell proliferation and increased cell death (apoptosis) in tumors in mice226
- Enhanced inhibition of cancer cell growth from treatment with 5-FU in rats227

Indole-3-carbinol supplements

- Reduced incidence and multiple occurrences per animal of colonic adenomatous polyps in mice228

L-glycine

- Decreased liver metastases tumor volume and microvascular density when combined with FOLFOX in animals229

Probiotics

- Suppressed colon tumor incidence/number and size and increased cell death (apoptosis) in animals230

Other therapies with preclinical evidence only for treating the cancer

- Cocoa
- Ginger

- L-carnitine
- Quercetin
- Vitamin K2

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

These therapies have exciting potential and/or proven benefits. However, some carry higher risks of side effects, interactions with other treatments and other adverse medical events than other therapies we review. Cautions are noted with each therapy, and we strongly urge you to consult your doctor before using these therapies—even over-the-counter drugs—for cancer treatment. We also note whether a prescription is needed or if a therapy is not widely available.

Group A: Good clinical evidence of efficacy

May be used in integrative protocols and programs

Aspirin

- Improved survival in general,231 but considerable variation in individual study findings depending on study specifics:
- Improved overall survival when used after diagnosis but not before diagnosis, and only in patients positive for COX-2 expression (which influences tumor invasiveness and inflammatory responses) and mutated PIK3CA tumors232
- Improved colorectal cancer-specific survival and lower odds of diagnosis with distant metastases with long-term regular use of aspirin (more than 15 times per month) before diagnosis; beginning regular aspirin use only after diagnosis improved survival compared with no aspirin use233
- Improved survival in those with wild-type BRAF tumors but not mutated BRAF tumors234 or with PI3K mutation235
- Improved all-cause and cancer-related survival at varying doses, regardless of body mass index236
- Improved survival for type II diabetes patients with stage 2 and 3 colorectal cancer treated with both aspirin and metformin237
- Improved survival in tumors with low PD-LI expression (which inhibits immune action against tumors) wth aspirin use with immunotherapy238
- Improved five-year progression-free survival and a lower risk of developing metastasis239
- Inhibited gene mutations which can contribute to uncontrolled proliferation of cells and also induced cell death (apoptosis), improving survival and reducing recurrence240
- Induced cell death (apoptosis), improving survival and reducing recurrence in metastatic colorectal cancer241
- Slightly higher mortality among elderly colorectal cancer patients taking daily low-dose aspirin242
- Slowed polyp progression in patients with hereditary nonpolyposis colorectal cancer243

- Increased rate of tumor downstaging with use during neo-adjuvant therapy (therapy prior to the main therapy)244 and during preoperative chemoradiation for rectal cancer245
- No improvements in toxicity or response rate (pathological complete response rate) in rectal cancer patients undergoing neo-adjuvant long-course radiation therapy246
- Significan cautions regarding gastrointestinal bleeding and other risks with use; see Cautions on our Aspirin and Non-steroidal Anti-inflammatory Drugs page
- Used in these programs and protocols:
    - Block program247
    - Chang strategies248

Chronomodulated therapies

- Higher rates of complete and partial remissions compared to those getting continuous infusion chemotherapy.249
- Prolonged median overall survival in men, but not always in women250
- Improved tumor response251 including longer median time to treatment failure compared to constant-rate infusion252
- Use of higher doses of 5-FU with greater objective response, progression-free survival and median survival in patients with previously untreated metastatic colorectal cancer253
- No difference in survival in four-day chronomodulated combination of 5-fluorouracil and oxaliplatin versus two-day FOLFOX2 (chemotherapy regimen containing folinic acid (leucovorin), fluorouracil, and oxaliplatin)254
- Improved tolerability of chemotherapy and near doubling of anticancer activity with oxaliplatin and 5-FU-leucovorin given through chronomodulated vs. constant-rate administration255
- Improved outcomes and survival with metastasis256
- Improved survival (compared to other studies) with chronotherapy compared to continuous infusion in a small study of people with stage 3-4 colon cancer, although the numbers were too small to draw conclusions257
- Optimal chronomodulated schedules corresponded to peak delivery rates at 1am or 4am for 5-fluorouracil-leucovorin, at 1pm or 4pm for oxaliplatin, and at 4pm for carboplatin.258
- Influenced all markers of enzyme activity (phenotype markers) important for tolerability and efficacy of fluoropyrimidine drugs259
- Notable preclinical evidence:
    - Findings of best times to administer specific chemotherapy drugs: oxaliplatin 1-4pm, 5-FU early morning before 6am, Irinotecan morning 6-9am260

Metformin

- Lower overall mortality and colorectal cancer-specific mortality.261

- May improve overall survival in colorectal cancer patients with metabolic syndrome262 or diabetes263
- Increased disease control rate at week 12 when combined with irinotecan264 or at week 8 with 5-fluorouracil265 in patients with measurable metastatic colorectal cancer
- Reversed the proliferation of colorectal cancer cells enhanced by d-(+)-glucose administration and considerably increased sensitivity to oxaliplatin chemotherapy266
- May be a useful adjuvant therapy, especially in colorectal cancer patients receiving radical radiotherapy.267
- Notable preclinical evidence:
    - Enabled normal SCID (severe combined immunodeficiency) mice not deficient in T cells to reject solid tumors and increased the number of tumor-infiltrating lymphocytes and protected them from cell death (apoptosis) and exhaustion268
    - May increase the efficacy of immunotherapy269
- Requires a prescription from a licensed physician
- Used in the Block program270

Statins

- Overall, most studies show improved survival (overall, progression-free, recurrence-free, disease-free survival) and prognosis, although differences are seen depending on the cancer treatment used and patient characteristics.
- Evidence of positive treatment effects:
- Decreased risk of all-cause mortality, and for all types of cancer combined, reductions in cancer-specific mortality and improvements in progression-free survival, recurrence-free survival and disease-free survival; improvements in recurrence-free survival were significantly greater with use after diagnosis than before diagnosis271
- Similar survival outcomes to patients mean BMI 24-25 treated with lifestyle modifications272 (Note: lifestyle modifications, such as the 7 Healing Practices, involve far fewer side effects and risks compared to statins.)
- Reduced all-cause and cancer-specific mortality with statin uses both before and after diagnosis in some reviews and meta-analyses273 and improved overall survival in a separate retrospective cohort review274
- Improved prognosis in large-scale cohort studies275
- Better prognosis of surgically resected colorectal cancer in one review,276 although another study found no differences in disease-free survival, recurrence-free survival or all-cause mortality in patients undergoing neoadjuvant chemoradiotherapy and resection for rectal cancer277
- Reduced proportion of late-stage (at diagnosis) colorectal cancer cases among users of lipophilic statins in a large retrospective study of women278 and a population-based case-control study279
- Higher rate of tumor downstaging (reduction in the cancer stage) with use during neoadjuvant therapy280

- A combination regimen of simvastatin, cetuximab and irinotecan showed promising safety and efficacy in KRAS-mutated colorectal cancer patients for whom irinotecan and oxaliplatin had failed.281
- Evidence of no improvement:
- No improved progression-free survival and overall survival in some analyses,282 perhaps due to poor trial design283
- Noteworthy preclinical evidence:
- Anticancer proliferation effects in resistant colorectal cancer cells when used with chemotherapy drugs; interfered with insulin-like growth factor 1 receptor (IGF-1R) signaling, which is known to promote cancer cell survival and proliferation; and other anticancer effects284
- Only natural statins (simvastatin, mevastatin and lovastatin) suppressed NF-kB activation. NF-kB, a group of proteins that help control cell growth and survival, may be excessive or overactive in some types of cancer cells, which may lead to cancer cell growth.285
- Pretreatment with lovastatin significantly increased cell death (apoptosis) induced by 5-fluorouracil (5-FU) or cisplatin in colon cancer cell lines.286
- Requires a prescription from a licensed physician
- Note significant cautions in our Statins page.
- Used in the Block program287

Group B: Limited clinical evidence of efficacy

May be used in integrative protocols and programs

Artemisinin derivatives and artesunate

- Worked against tumor proliferation (antiproliferative) in a small trial288
- A 2018 review of clinical artesunate and artemisinin derivatives did not find efficacy in the treatment of colorectal cancer.289
- Notable preclinical evidence:
    - Tumor growth delay and tumor shrinkage in mice grafted with human colorectal cancer cells290
    - Dihydroartemisinin (DHA) sensitized resistant cells to 5-FU.291
    - DHA increased the rate at which doxorubicin inhibits tumors, with a further increase if DHA and doxorubicin were co-encapsulated into mannosylated liposomes.292
    - 10-(4-phenyl-1H-1,2,3- triazol)-artemisinin (5a) controlled acquired drug resistance and recovered the anticancer effect of paclitaxel on cancer cells.293
- Note cautions in our Artemisinin and Artesunate page.
- Used in the Parmar & Kazcor treatment plans294

Cimetidine (Tagamet)

- May improve survival in patients with colorectal cancer,295 such as when used as adjuncts (supplementary therapy) to surgery intended as a cure,296 although not all studies found benefit297
- May be more effective in those with less tumor burden and better immune function and in cancers that are more likely to trigger immune responses (have a higher antigenic potential)298
- Increased response of tumor-infiltrating lymphocytes when used 10 days before and seven days after surgery299
- May reduce the immunosuppressive effect of surgery in Dukes Stage A, B and C tumors
- Noteworthy preclinical evidence:
- Worked against proliferation and adhesion of cancer cells and increased production of antitumor cytokines300
- Reduced formation of blood vessels to supply tumors (angiogenesis)301
- Used in these programs and protocols:
    - Block program302
    - Chang strategies303

Chloroquine

- Limited evidence of chloroquine's efficacy in overcoming resistance to chemotherapy in colorectal cancer patients304
- Noteworthy preclinical evidence:
- Potentiated (enabled/enhanced) anticancer effect of 5-fluorouracil on colon cancer cells305
- Inhibited autophagy (cell self-cleaning) and enhanced apoptosis (cell death) in colorectal cancer cells when added to 5-fluorouracil (5-FU) and oxaliplatin, when used with bortezomib, or in combination with 5-FU and radiation therapy306
- Requires a prescription from a licensed physician

Copper chelation with tetrathiomolybdate (TM) and other substances

- No notable improvements in time to progression, but also no increase in toxicity or interference with effects of irinotecan, 5-fluorouracil, and leucovorin in a small clinical trial of in patients with advanced metastatic colorectal cancer307
- TM showed anti-angiogenic activity (prevents the formation of new blood vessels) while avoiding clinical copper deficiency.308
- Noteworthy preclinical evidence:
- Antitumor activity in human colon cancer cells grafted onto mice309
- Affected proliferation, survival and migration in colorectal cancer cells with BRAF mutation, a gene mutation which may increase the growth and spread of cancer cells. Copper chelation also decreased the cloning potential of BRAF cells otherwise resistant to drugs targeting the BRAF mutation310
- Melon extracts, especially melon peel aqueous extract, showed copper-chelating properties in lab studies.311

- Copper chelators plus iron chelators combined with DHA and 5-FU in colorectal cancer cells overcame drug resistance through increased cell death (apoptosis).312
- Used in these programs and protocols:
    - Block program313
    - Parmar & Kazcor treatment plans314
    - BCCT is aware of several reputable integrative oncologists seeing positive responses to using copper chelation in patients with advanced solid tumors.

Nelfinavir (Virocept)

- May improve tumor regression compared to radiotherapy alone315
- May reduce tumors when used with radiotherapy in combination with capecitabine316
- Noteworthy preclinical evidence:
- Inhibited tumor growth in mice317 . and cell studies318
- Note significant cautions and interactions with other drugs: ask your doctor or pharmacist.

Nonsteroidal anti-inflammatory drugs (NSAIDs) other than aspirin (MedicineNet)

- No improvement in disease-free survival or overall survival among people with stage 3 colon cancer with three years of celecoxib (Celebrex) added to standard adjuvant fluorouracil, leucovorin, and oxaliplatin (FOLFOX) in a large randomized trial319
- Improved overall survival in KRAS wild-type mutations but not KRAS-mutated patients when combined with cetuximab targeted therapy320
- Inconclusive clinical results of survival benefit overall, but improved survival with tumors with low expression of PD-LI (programmed cell-death ligand, a molecule on the surface of tumor cells that inhibits the antitumor function of T cells)321
- Noteworthy preclinical evidence:
- Reduced resistance to chemotherapy in colorectal cancer322 .
- Improved antitumor immune response and tumor eradication when combined with anti-PD1 monoclonal antibody323
- Antiproliferative effects (reduced tumor growth) from diclofenac in animal studies324
- Significant cautions regarding gastrointestinal bleeding and other risks with use

Rapamycin (sirolimus)

- High response and cancer control rates when rapamycin and hydroxychloroquine were added to metronomic chemotherapy (also called low-dose chemotherapy) for refractory metastatic solid tumors in a small group of patients who didn't respond to first-line metronomic chemotherapy325
- Tolerated by most patients when used with bevacizumab, at lower cost than other mTOR inhibitors, but without significant treatment effects in patients with pathologically confirmed advanced solid tumors for which standard curative or palliative measures either do not exist or were no longer effective326
- Noteworthy preclinical evidence:

- Enhanced response to erlotinib, inhibiting cell growth pathways in cell and animal models327
- Requires a prescription from a licensed physician
- Note cautions when using after surgery.

Group C: Promising preclinical evidence only

Bisphosphonates (Cancer Research UK), including clodronate (Canada) and zoledronic acid (Reclast, Zometa),

- Clodronate liposomes decreased tumor numbers in mice.328
- Zoledronic acid reduced cell viability and growth.329
- Zoledronic acid or a derivative (another drug made from zoledronic acid) regulated cell self-cleaning (autophagy) and induced cell death (apoptosis) in colorectal cancer cells330
- Note several side effects.

Diets and Metabolic Therapies

Short-term fasting (noteworthy preclinical evidence)

- As effective as chemotherapy in delaying the progression of a wide range of cancers in animals331
- Reduced tumor progression in mice with complete fasts of one to two days or alternating fasting and non-fasting days332
- Synergistic effect with vitamin C in delaying tumor progression in mice with colorectal cancer with the KRAS gene mutation333
- Enhanced the effect of virus-mediated cell killing in colorectal cancer cells while protecting normal colon cells334
- Alternate-day fasting inhibited tumor growth in mice without causing weight loss.335
- Note cautions.

Manipulative and Body-Based Methods

Acupuncture and Electroacupuncture

- Reduced average tumor size and other indicators of cancer using nanoporous needles in animals (needles that have micro/nano-scale pores on their surface)336

Therapies Using Heat, Sound, Light or Cutting-edge Radiotherapy

Hyperthermia

- Local or regional hyperthermia:
    - Improved overall survival time of patients with liver metastases from colorectal cancer compared to chemotherapy alone337

    - "Excellent survival outcomes in optimally selected patients" with colorectal cancer who have peritoneal metastases treated with systemic chemotherapy, then cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). Both oxaliplatin and mitomycin C had comparable effectiveness when given in the intraperitoneal cavity. (Report on a presentation at the ESMO 22nd World Congress on Gastrointestinal Cancer)338
    - Greater rates of complete response and regression of the primary tumor339
    - No improved survival and an increased risk of adverse events in colorectal cancer patients when adding HIPEC to cytoreductive surgery compared with receiving cytoreductive surgery alone340
- Whole-body hyperthermia:
    - Improved response to chemotherapy and potentially improved survival341

Managing Side Effects and Promoting Wellness

Side effects of the cancer and of treatments can dramatically impact your quality of life. A 2009 review summarizes: “Although issues and symptoms were most prominent during the first three years, long-term effects of treatment can persist and include fatigue, sleep difficulty, fear of recurrence, anxiety, depression, negative body image, sensory neuropathy, gastrointestinal problems, urinary incontinence, and sexual dysfunction.”345 Therapies that address side effects can greatly improve your well-being and improve life for you and your caregivers.

Conventional Treatments

Pulsed low-dose rate radiation therapy (PLDR-RT) delivers conventional radiation doses in pulses of small doses with intermittent pauses. A small study involved PLDR-RT for rectal and other cancers of the pelvis. Of the 50 percent of patients who reported pain at the local site before treatment, 68 percent reported an improvement in pain after PLDT-RT.346

Natural Products

Group 1: Good clinical evidence of efficacy & safety, easy access

These therapies may be widely used in integrative cancer protocols and traditional medical systems.

Astragalus

- Improved quality of life and reduced adverse reactions—including nausea and vomiting, diarrhea, neurotoxicity, neutropenia (low count of white blood cells called neutrophils), anemia, thrombocytopenia (low count of platelets) and leukopenia (low count of white blood cells)—when used during chemotherapy in treating colorectal cancer347

- Reduced incidence of chemotherapy-induced neutropenia (low count of white blood cells called neutrophils, leading to increased susceptibility to infection) when administered orally with oxaliplatin348
- Improved appetite, sleep and quality of life, reduced fatigue, pain, inflammation, nausea and vomiting with advanced metastatic cancer using IV (intravenous) astragalus polysaccharides349
- Reduced chemotherapy-induced nausea and vomiting with oxaliplatin; regulation of gastrointestinal motility and gastroprotective effects350
- Reduced fatigue and immune suppression caused by chemotherapy351
- Reduced diarrhea related to chemotherapy for colorectal cancer352
- Protected nervous system tissue353 and relieved pain from nerve damage induced by oxaliplatin without affecting the anticancer effect of chemotherapy354
- Reduced incidence and severity of chemotherapy-induced peripheral neuropathy and improved nerve function and functional performance in people with various types of cancer (mostly gastrointestinal/colorectal), in some studies improving the response when used with western analgesics355
- Reduced neurotoxicity when used during chemotherapy for colorectal cancer356

Curcumin

- Improved quality of life in patients with solid tumors receiving standard chemotherapy regimens and a bioavailability-enhanced curcumin preparation in small studies357
- Increased body weight and prevented weakness and wasting (cachexia) in colorectal cancer patients after diagnosis and before surgery358 and in general.359
- Reduced several side effects of chemo- and radiotherapy, including mucositis, mouth and throat ulcers, swallowing problems, nausea and vomiting), swelling (erythema), skin lesions and weakness, and was protective of the liver360
- Reduced treatment symptoms such as nausea, constipation, diarrhea, soreness and ulceration with the Meriva® formulation361
- Reduced pain from chemo- and radiotherapy362
- Reduced incidence of adverse events (at least grade 4) and occurrence of increased serum creatinine (an indicator of kidney toxicity) in people with colorectal cancer363

Ginger

The effects of ginger in your diet are discussed above in Eating Well.

- Protected from and worked against toxicities from chemicals and radiation364
- Reduced nausea and vomiting from chemotherapy and following surgery365

L-glutamine, also known as glutamine

During chemotherapy:

- Reduced incidence and severity of oxaliplatin-induced peripheral neuropathy with no significant impact on response to chemotherapy366

- Reduced severity of peripheral neuropathy associated with paclitaxel treatment at high doses (10 g orally, three times a day for 4 days)367 but not low doses (500 mg three times a day)368
- Reduced some side effects induced by chemotherapy such as gut mucositis (inflammation in the lining of the digestive tract) and diarrhea, and improved wound healing after surgery369
- Reduced duration of diarrhea but no improvement in severity of diarrhea during chemotherapy in a 2012 meta-analysis370
- Decreased nausea/vomiting and diarrhea during chemotherapy with intravenous alanyl-glutamine dipeptide use371
- Reduced oral mucositis,372 diarrhea and average number of loperamide tablets taken during treatment with 5-Fluorouracil (5-FU)373
- No significant decrease in grade 3–4 non-hematological toxicities (toxicities other than a decrease in blood cell production) among patients undergoing chemotherapy374

During radiation or combination therapy:

- Reduced severity of radiation-induced diarrhea and reduced need for treatment breaks with 15 g of oral glutamine three times daily,375 but no improvement with 30 g per day in three doses during preoperative radiochemotherapy376
- Failed to prevent the development of enteritis (inflammation of the small intestine) during radiotherapy377
- BCCT advisor Keith Block, MD, provides guidance to discontinue after treatment ends.378

Melatonin

- Prevented or minimized the unfavorable effects of radiotherapy on reduced blood cell count in rectal cancer patients379
- Reduced frequency of chemotherapy-induced side effects:380
- Weakness (asthenia)
- Low blood platelet count (thrombocytopenia)
- Inflammation of the mouth and lips (stomatitis)
- Damage to the heart (cardiotoxicity)
- Damage to nerves (neurotoxicity)
- Loss of strength and energy
- Reduced toxicity and the typical postsurgical reduction in lymphocytes when administered with low-dose interleukin-2 before surgery for gastrointestinal tract tumors381

Omega-3 fatty acid supplements

The effects of omega-3s in your diet are discussed above in Eating Well.

- Reduced incidence of peripheral neuropathy and promoted weight maintenance or gain during cancer treatment, and improved scores of physical function and global health status382

- Promoted body weight maintenance during chemotherapy383 or weight gain384 and reduced muscle loss385
- Improved quality of life and chemotherapy-related side effects including appetite loss, fatigue, pain, nausea and vomiting and diarrhea with a combination omega-3 fatty acid and strain-specific probiotic386
- Reduced postoperative infectious complications and hospital stay after colorectal cancer surgery in one study387 but no improvement in infectious or non-infectious postoperative complications in another388
- Eicosapentaenoic acid (EPA) alone
- Increased weight and improved scores of health-related quality of life, with a trend toward fewer interruptions of chemotherapy treatment389
- Increased mean weight and energy levels in an uncontrolled trial of colorectal cancer patients undergoing chemotherapy with folinic acid, 5-fluorouracil, irinotecan (FOLFIRI)390
- Reduced deterioration of nutritional status resulting from antineoplastic therapies (therapies to block the formation of neoplasms) by improving calorie and protein intake391

Probiotics

- Reduced incidence of diarrhea induced by chemoradiotherapy, especially grade 2 or higher392
- Reduced the portion of colorectal cancer patients experiencing irritable bowel symptoms or symptoms of depression, and improved function-related quality of life and cancer-related quality of life scores in a small trial393
- Conflicting findings on whether the use of prebiotics, probiotics or synbiotics at the time of surgery in patients undergoing colorectal cancer surgery reduces the development of infectious complications394

Group 2: Good clinical evidence of efficacy & safety, limited access

Some may require a prescription, for example.

Medical cannabis and cannabinoids

- A 2018 review from the National Academy of Sciences, Engineering and Medicine drew these conclusions:395
- Effective for treating pain in adults and chemotherapy-induced nausea and vomiting (Conclusive or substantial evidence)
- Improved secondary sleep disturbances (moderate evidence)
- Insufficient evidence of improved appetite or anxiety
- Improvements in several side effects, including these in a prospective study in Israel:396
- Sleep problems
- Pain
- Weakness and fatigue

- Digestion problems
- Anxiety and depression
- Nausea and vomiting
- Lack of appetite
- No improvement in reducing pain, sleep problems or opioid use among cancer patients with moderate and severe pain despite opioid therapy in a separate 2019 review from Germany and Canada397
- Access varies by country or US state, with moderately easy access in some areas and no or very limited legal access in others

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

- Reduced neurotoxicity during oxaliplatin/5-fluorouracil/leucovorin (FOLFOX) regimen without impairing the activities of the the drugs in the body (pharmacokinetics) or the formation of platinum-DNA adducts (which stop cancer cells from dividing)398
- Prevented severe chronic neurotoxicity induced by chemotherapy399
- Used in the Block program400

Magnesium

Evidence regarding magnesium in your diet is listed above in Eating Well.

- Deficiency is associated with personality changes including apathy, depression, agitation, confusion, anxiety, panic attack disorders, disrupted sleep patterns and delirium;401 supplementation reduces anxiety in animals and people402
- Used in the Block program403

Mistletoe (European)

- Lower cancer-related fatigue404
- Fewer reactions related to adjuvant (supplemental) therapy and fewer persisting symptoms405
- Fewer adverse events and lower rates of discontinuation of standard oncological treatment406
- Can be highly toxic if used inappropriately; see Cautions in the full review
- Used in these programs and protocols:
    - Alschuler & Gazella complementary approaches407
    - McKinney protocols408
    - Parmar & Kazcor treatment plans409

N-acetylcysteine

- Reduced the incidence of oxaliplatin-induced neuropathy in colon cancer patients in two small trials,410 but reviews find insufficient evidence to recommend it for treating or preventing chemotherapy-induced peripheral neuropathy (CIPN).411

- Used in the Block program412 for reducing peripheral neuropathy

Group 4: Potential significant benefit, but either limited clinical evidence of efficacy or significant cautions

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Combinations of therapies

- Astragalus membranaceus and Jiaozhen
    - Protected against intestinal barrier dysfunction in postoperative colorectal cancer patients413
- Calcium and magnesium (intravenous)
    - Two studies found positive effects:
    - Delayed time to onset of grade 2 sensory neurotoxicity and reduced chronic, cumulative sensory neurotoxicity and acute muscle spasms induced by oxaliplatin (FOLFOX) in adjuvant colon cancer414
    - Outcomes with calcium and magnesium infusions among patients treated with oxaliplatin plus 5-fluorouracil and leucovorin for advanced colorectal cancer:415
    - Reduced incidence and intensity of acute oxaliplatin-induced symptoms
    - Possibly delayed cumulative neuropathy and more rapid recovery from neuropathy
    - Lower rate of treatment termination for any type of toxicity
    - Less severe and prolonged weakness or lack of energy (asthenia)
    - Higher likelihood of maintaining body weight
    - But a review of these studies concluded not enough evidence showed reduced oxaliplatin-induced neurotoxicity416
- Kangai injection (KAI, ginseng, Astragali radix and kushen)
    - Reduced neurotoxicity when used during chemotherapy for colorectal cancer417
- LC09 (Astragalus membranaceus, flowers carthami, lithospermum, Geranium wilfordii, and Radix angelicae)
    - Decreased pain in colorectal cancer patients with chemotherapy-associated hand-foot syndrome418
- Medroxyprogesterone or megestrol acetate, eicosapentaenoic acid, L-carnitine and thalidomide
    - Increased lean-body mass, decreased resting energy expenditure, improved fatigue and appetite, improved performance status in patients with cachexia (weakness and wasting)419
- Quxie Capsule, a combination of traditional Chinese medicine therapies
    - Improved symptoms and quality of life in a small study420

Curcumin

- Reduced several side effects of chemo- and radiotherapy; protective of the liver421
- Improved health-related quality of life,422 including in patients with solid tumors under standard chemotherapy regimens423
- Prevented cachexia (weakness and wasting) and increased body weight in colorectal cancer patients after diagnosis and before surgery424
- A topical turmeric-based cream reduced radiotherapy-induced dermatitis.425
- Notable preclinical evidence:
    - Protective or nerves,426 preventing the initiation and development of peripheral neurotoxicity and reducing oxaliplatin-induced neurotoxicity427

Fermented wheat germ extract

- Improved quality of life428 and improved or reduced side effects of conventional treatment429 in limited clinical trials

L-carnosine (WebMD)

- Reduced oxaliplatin-induced peripheral neuropathy in colorectal cancer patients430

Selenium supplements

- Reduced blood cell toxicity but no effect on kidney or hearing toxicity during cisplatin use431

Vitamin B supplements

- Some evidence of reduced chemotherapy-induced peripheral neuropathy (CIPN), which may vary according to the specific B vitamin used432
- Reduced pain with methylcobalamin, a form of vitamin B12433

Vitamin C (intravenous)

- Improved global health/quality of life—including physical, role, emotional, and cognitive functions—and lower scores for fatigue, nausea and vomiting, pain and appetite loss among terminal cancer patients434 and newly diagnosed cancer patients435
- Decreased pain following laparoscopic colectomy and a case report of reduced symptoms from standard therapy with intravenous ascorbic acid436

Vitamin E supplementation

- Reduced cisplatin-induced neuropathy, but no benefits seen with taxane neuropathy, oxaliplatin-induced peripheral neuropathy, anthracycline cardiotoxicity, or general carboplatin toxicity437
- Reduced radiotherapy toxicity438

Group 5 Especially promising preclinical or emerging clinical evidence of efficacy and safety

Aged garlic extract

The effects of garlic in your diet are discussed above in Eating Well.

- Reduced damage of the small intestine from methotrexate in rats439
- Caution regarding increased risk of colorectal cancer with use
- Used in the Block program440 for radiation enteritis

Grape seed extract

- Reduced damage to the lining of the colon (mucositis) in rats441

L-glycine

- Diminished liver and kidney injury caused by toxicants and drugs, including chemotherapy-induced liver injury, and protected stomach lining (gastric mucosa) against ulcers induced by chemicals or stress442

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

These therapies have exciting potential and/or proven benefits. However, some carry higher risks of side effects, interactions with other treatments and other adverse medical events than other therapies we review. Cautions are noted with each therapy, and we strongly urge you to consult your doctor before using these therapies—even over-the-counter drugs—for cancer treatment. We also note whether a prescription is needed or if a therapy is not widely available.

Group A: Good clinical evidence of efficacy

May be used in integrative protocols and programs

Chronomodulated therapies

- Reduced rate and severity of adverse reactions compared to those getting continuous infusion chemotherapy,443 including greatly reduced rate of severe damage to the intestinal lining (mucosal toxicity) and halved rate of functional impairment from peripheral sensitive neuropathy444
- Reduced severe inflammation of the mouth and lips (stomatitis)445
- Reduced rate and severity of adverse reactions while achieving higher rates of remissions (both complete and partial) compared to those getting continuous infusion chemotherapy446
- Better quality life and less fatigue in metastatic colorectal cancer patients with normal 24-hour rest/activity rhythms than those with altered rhythms447
- Patients' ability to tolerate the drug schedule varied from women to men448
- Notable preclinical effects:
- Timing of cisplatin and carboplatin influenced whether male mice developed low counts of white blood cells (leukopenia), bone marrow lesions and cortical tubular necrosis (death of tissue in the outer kidney)449

Metformin

- Lower rate of grade 2 and 3 neuropathy, lower pain scores and lower markers of oxidative stress and heightened sensitivity to pain (hyperalgesia)450
- Notable preclinical evidence
    - Reduced loss of paw sensitivity and protected peripheral-nerve endings in mice451
    - Prevented mental (cognitive) impairment due to the chemotherapy drug cisplatin452
- Requires a prescription from a licensed physician

Group B: Limited clinical evidence of efficacy

May be used in integrative protocols and programs

Aspirin

- Reduced events related to vascular disease (abnormal condition of the blood vessels), including blood clots in deep veins (venous thromboembolism)453
- Significan cautions regarding gastrointestinal bleeding and other risks with use; see Cautions on our Aspirin and Non-steroidal Anti-inflammatory Drugs page
- Used in the Block program454

Bisphosphonates

- Zoledronic acid decreased bone pain and improved quality of life when combined with radiotherapy to treat painful bone metastases from colorectal and other cancers in a small study455
- Note several side effects.
- Requires a prescription from a licensed physician

Cimetidine (Tagamet HB)

- Reduced the suppression of immune function that typically follows surgical resection456
- Notable preclinical evidence: reduced risk of kidney toxicity (nephrotoxicity) in mice without reducing the antitumor effects of cisplatin457
- Note cautions and drug interactions: ask your doctor or pharmacist

Statins

- Use near the time of surgery may reduce anastomotic leaks (leaking where the colon segments were joined after removing the tumor) after elective colectomy458
- Requires a prescription from a licensed physician
- Note cautions.
- Used in the Block program for colorectal cancer459

Diets and Metabolic Therapies

Short-term fasting

- Reduced chemotherapy-related fatigue, weakness, and gastrointestinal side effects while fasting without impairing the effect of chemotherapy460
- Increased protection against stressors including toxics in patients who fasted for 48 hours or longer around the time of platinum-based chemotherapy461
- Limited weight loss and toxicity to the heart and cardiovascular system related to chemotherapy462
- Reduced DNA damage in white blood cells (leukocytes) in patients who fasted for 48 hours or longer around the time of platinum-based chemotherapy463
- Noteworthy preclinical evidence:
    - Protected mice against irinotecan side effects464
    - Protected normal cells from the toxic effects of chemotherapy drugs while sensitizing cancer cells to the treatment465
    - Reduced suppression of immune function and mortality caused by chemotherapy and promoted regenerative effects on stem cells in cell and animal studies466
- Note cautions
- Used in the Block program for colorectal cancer467

For people having significant side effects—especially gastrointestinal—from chemotherapy, naturopathic oncologist and BCCT advisor Lise Alschuler recommends fasting for 48 hours, from after dinner on the day before chemotherapy, through the day of chemo and the day following. This can be a water fast (which includes coconut water and vegetable broths), or you can eat up to 600 calories per day of vegetable soup and/or low-carb vegetables. She stresses the importance of your being motivated to fast for success, and also that fasting during chemotherapy should be cleared with your treating oncologist. You should modify or stop the fast if you become dizzy or weak (in which case you can try adding boiled eggs or nuts), or if you feel worse than if you had eaten.

Mind-Body, Spiritual and Consciousness-changing Approaches

Guided imagery

- Relaxation with guided imagery can reduce anxiety, pain and narcotic use following colorectal surgery and increase patient satisfaction.468
- More effects of guided imagery with cancer in general are described on our Guided Imagery page.

Manipulative and Body-Based Methods

Acupuncture and electroacupuncture

- Improved peripheral nerve symptoms and function, lowered incidence of chemotherapy-induced peripheral neuropathy, and reduced the need to for symptom mitigation in small studies469
- Reduced reported pain and toxicity to nerves from chemotherapy, and improved quality of life in an uncontrolled pilot study of ultrasound acupuncture;470 a related clinical trial is investigating the effectiveness and safety with colorectal cancer patients471
- Enhanced the effectiveness of ondansetron in reducing nausea, vomiting, abdominal distention and diarrhea, reduced length of hospital stay and improved wellness in patients receiving hyperthermic intraperitoneal chemotherapy after surgery472

Reducing Risk

Reducing the risk of developing cancer or the risk of recurrence

Risk Factors

These factors increase risk of colorectal cancer:473

- Inflammation
- Abnormal blood glucose (glycemia)
- Increasing age
- Family history of colorectal cancer
- Race, with African-Americans at increased risk
- History of abdominal radiation
- Diabetes mellitus and insulin resistance
- Moderate or severe famine before adulthood in women
- Metabolic syndrome, defined by having several of these conditions:474
- Increased blood pressure
- High blood sugar
- Excess body fat around the waist
- Abnormal cholesterol or triglyceride levels

Creating Healthy Habits: Lifestyle Associations

The role of the 7 Healing Practices in reducing risk is described above. Further lifestyle choices also relate to your risk of colorectal cancer:475

- Body fat/obesity, including high body mass index (BMI) early in life, especially in men. Risk increases 2 to 3 percent with each increased unit of BMI. Even among people considered of normal weight and not overweight (BMI < 25), increased body fat was associated with increased risk of colon cancer, but only in men).476 Obesity is also associated with worse cancer outcomes, such as higher risk of recurrence of the primary cancer or mortality.
- Drinking two or more alcoholic drinks daily increases risk of developing colorectal cancer, especially among men. Moderate alcohol consumption (2-3 drinks) increases risk 20 percent, and higher consumption may increase risk up to 50 percent.

- Smoking tobacco increases risk of colorectal and other cancers; risk increases with the amount of smoking, similar to alcohol consumption.
- Night shift work is correlated with a 30 percent or higher increased risk of colorectal cancer.
- Combination hormone-replacement therapy in women decreases risk, but must be weighed against other health risks associated with use. Colorectal cancers found in women taking hormone therapy after menopause may be at a more advanced stage.

Natural Products

Group 1: Good clinical evidence of efficacy & safety, easy access

These therapies may be widely used in integrative cancer protocols and traditional medical systems.

Calcium supplements (About Herbs)
Evidence regarding calcium in your diet is listed above in Eating Well.

- Decreased risk of colorectal cancer:
- The Continuous Update Project Expert Report considers the evidence for calcium in reducing risk to be strong.477 This conclusion is supported by a meta-analysis combining 15 studies478 even though some randomized controlled clinical trials following use for up to 11 years have failed to show a protective benefit.479

Magnesium supplements (About Herbs)
Evidence regarding magnesium in your diet is listed above in Eating Well.

- Reduced risk of colorectal cancer, especially colon cancer, with higher intake of magnesium from diet and/or supplements480

Medicinal mushrooms

- Turkey tail mushrooms:
    - PSK (an extract of turkey tail mushrooms) reduced recurrence of colorectal cancer when used with oral Tegafur/Uracil481
- Reishi mushrooms
    - Suppressed development of colorectal adenomas in patients with prior adenomas.482
- Notable preclinical evidence: Inhibited proliferation of human colorectal cancer cells in mice483

Vitamin B supplements

- Vitamin B2:
    - Reduced colorectal cancer risk484
- Vitamin B6 (About Herbs)

- Decreased risk of colorectal cancer with increased intake from diet and supplements485

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Combination therapies

- Curcumin and quercetin
  - Suppressed adenomas in patients with familial adenomatous polyposis (FAP), a risk factor for colorectal cancer486
  - Decreased polyp numbers and size487
  - Used in the Alschuler & Gazella complementary approaches488

Curcumin

- Blocks or reduces risk of cancer development489
- Reduced aberrant crypt foci (ACF) formation in smokers; ACF are one of the earliest changes that can be seen in the colon that may lead to cancer490
- Notable preclinical evidence:
  - Reduced cancer incidence in animal studies491
  - Diminished aberrant crypt foci (ACF), intestinal polyps, and incidence and number of colon adenomas and adenocarcinomas in rodents492
  - Reduced cancer stem cells and modulated communication between fibroblasts (connective tissue cells that make and secrete collagen proteins) in the tumor microenvironment and cancer stem cells493
  - Anticancer effects include inhibiting cell proliferation, invasion, migration, formation of blood vessels to supply tumors (angiogenesis) and metastasis; inducing cell cycle arrest and death (apoptosis)494
- Used in these protocols and programs:
  - Alschuler & Gazella complementary approaches495
  - Block program496
  - McKinney protocols497

Green tea extracts/EGCG

The effects of drinking tea are discussed above in Eating Well.

- Inhibited tumor stem cell proliferation, prevented tumor production, and reduced risk of recurrence after surgery498
- Prevented the development and progression of precancerous lesions, such as colorectal adenomas,499 and reduced incidence of metachronous (not concurrent) adenomas after colorectal adenomas were removed500
- Notable preclinical evidence:
  - Protected animals from colon cancer induced by azoxymethane501

    - Inhibited polyp formation in animals and suppressed small intestinal tumor formation in mice502
    - Inhibited tumor incidence, with near-normal survival rate and restoration of normal colon architecture in rodents503
    - Inhibited pre-cancerous polyps and development of colon cancer in mice fed a high-fat diet504
    - Inhibited cancer development in intestinal, colon and gastric cancer in preclinical studies505
- Used in these Programs and Protocols:
    - Alschuler & Gazella complementary approaches506
    - Block program507
    - Lemole, Mehta & McKee protocols508

- Multivitamin supplements
    - Might decrease the risk of colorectal cancer,509 although use was not related to colorectal cancer risk in a large study of US women aged 45 years or more.510
    - Used in the Block program511

Omega-3 fatty acid supplements

The effects of omega-3s in your diet are discussed above in Eating Well.

- Decreased risk of colon cancer with fish oil supplements,512 especially in men, but an increased risk was found with individuals with high genetic risk513
- Reduced number and size of rectal adenomas514
- Reduced risk of colon cancer with consumption of omega-3 long-chain polyunsaturated fatty acids (LCPUFAs) and an omega-6/omega-3 ratio of 2-4:1515
- EPA alone:
- Reduced number and size of polyps in patients with familial adenomatous polyposis with eicosapentaenoic acid (EPA) alone516
- No reduction in the proportion of patients with at least one colorectal adenoma in patients with sporadic colorectal neoplasia, used either with or without aspirin, compared with a placebo517
- Used in these programs and protocols:
    - Block program518
    - Lemole, Mehta & McKee protocols519
    - McKinney protocols520

Probiotics

- Preliminary but mixed evidence that probiotic therapy may decrease the risk of developing colorectal cancer521 with different effects from different species522
- As reported above in Eating Well, yogurt consumption reduced risk of conventional colorectal adenoma, especially adenomas with high malignant potential, in men. Probiotics in yogurt are thought to contribute to this effect.523

- Notable preclinical evidence: protected mice against colorectal cancer development with Lactobacillus casei BL23524 and histidine decarboxylase (HDC) Lactobacillus reuteri525
- Used in these programs and protocols:
    - Block program526
    - McKinney protocols527

Resveratrol

- Inhibited a major risk factor for colon cancer development in normal linings of the colon (colonic mucosa) but did not inhibit colon cancer in a small study of colon cancer patients528
- Used in these programs and protocols:
    - Alschuler & Gazella complementary approaches529
    - Block program530

Vitamin D

- Blood levels:
    - Increased risk of cancer with poor vitamin D status531
    - Lower risk of colorectal adenomas and recurrent adenomas with higher circulating 25(OH)D levels;532 the impact of vitamin D status is related to calcium intake533
- Supplement use:
    - Lower risk of colorectal cancer with increased intake of vitamin D, both through diet and with supplements534
    - Lower risk of incidence and recurrence of colorectal adenomas with vitamin D intake; combined calcium and vitamin D supplementation reduced risk of colorectal cancer recurrence,535 but no conclusive evidence that use of supplements alone reduces risk.536 In one study, estrogen therapy interacted with this benefit, showing benefit only in women not undergoing estrogen therapy.537
    - Research in animals shows that supplementation increases 25(OH)D levels,538 but no conclusive evidence shows that use of supplements reduces risk in humans.539
- Used in the Alschuler & Gazella complementary approaches540

Vitamin E supplements

- Serum levels:
    - Patients with colorectal cancer showed lower concentrations of serum vitamin E compared with hospital-based controls in a meta-analysis.541
- Supplement use:
    - The specific tocopherols within supplements may have different effects. Most supplements contain α-tocopherol, while a γ-tocopherol-rich mixture of

tocopherols inhibits growth of colon and other types of tumors in animals542 and in epidemiological studies543
    - Reduced risk of colorectal cancer in women taking unspecified forms of vitamin E supplements544 but not in men taking 400 IU/day of all-rac-α-tocopheryl acetate (see the study for an analysis of whether the correct form was used)545 in large studies
    - Other reviews and a meta-analysis concluded no reduced risk with vitamin E or other antioxidants546 (but again, the specific forms of vitamin E may have varying effects).
    - No reduced risk of adenoma occurrence547
- Used in these programs and protocols:
    - Lemole, Mehta & McKee protocols,548 using mixed tocopherols and tocotrienols
    - McKinney protocols,549 using mixed tocopherols with gamma and delta forms

Group 4: Potential significant benefit, but either limited clinical evidence of efficacy or significant cautions

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Fermented wheat germ extract

- Reduced likelihood of colorectal cancer recurrence and new metastatic disease occurrence550

Selenium

- Decreased colon cancer risk with elevated selenium intake in observational studies551 . but only a marginal decrease in a clinical trial; biggest effects were seen in males and in former smokers. Benefit was seen only for those with lower plasma selenium concentrations before supplementation552

Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Astragalus and other saponins

- Prevented gastrointestinal lesions in animals from progressing into cancer553

Combinations of therapies

- Resveratrol and grape seed extract:
    - Suppressed tumor incidence in mice similar to sulindac (a nonsteroidal anti-inflammatory drug, see below) without any gastrointestinal toxicity554

Ginger

The effects of ginger in your diet are discussed above in Eating Well.

- Reduced early markers in the development of colorectal canceramong healthy adults555
- Anticancer effects (antitumor, reduced proliferation, reduced invasion) in preclinical studies, with limited clinical evidence556
- Nanoparticles derived from edible ginger prevented cancer associated with colitis in animal studies.557

Grape seed extract

- Inhibited cancer proliferation and enhanced cell death (apoptosis) to prevent cancer development in animals558
- Prevented a pre-cancerous condition (aberrant crypt foci) induced by chemicals in rats559
- Decreased formation, total number and size of adenomatous polyps in mice560

Other therapies with preclinical evidence only for reducing risk

- Alpha-lipoic acid
- Quercetin (but see use with curcumin in Combination therapies in Group 3)

Group 6: Evidence of no efficacy or may be dangerous

Aged garlic extract

The effects of garlic in your diet are discussed above in Eating Well.

- Elevated risk of colorectal cancer with garlic pills561

Beta-carotene supplements

The effects of foods containing beta-carotene are discussed above in Eating Well.

- Increased risk of colorectal adenoma and overall mortality in the general population562

Folic acid

- No convincing evidence of reduced risk of colorectal cancer or adenomas in average-risk or high-risk populations; one randomized controlled trial found an increase in advanced adenomas with use563

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

Group A: Good clinical evidence of efficacy

May be used in integrative protocols and programs

Aspirin

- Recommended by the US Preventive Services Task Force for primary prevention of colorectal cancer564

- Reduced risk of colorectal cancer565 including in people with hereditary colorectal cancer (Lynch syndrome)566
- Prevented or reduced colorectal adenoma recurrence567
- May reduce recurrence of adenomas and incidence of advanced adenomas in individuals with an increased risk of colorectal cancer568
- Risk reduction may depend on dose, and may interact with height, weight and age of the individual;569 no reduced risk was seen among individuals aged 65 years or older,570 while another study found reduced risk in those over 70 only if use was initiated when younger571
- Notable preclinical evidence:
    - Reversed or inhibited the activity of platelets to promote cancer cell proliferation and metastasis572
    - Reduced cancer cell proliferation through the modulation of an oncoprotein in cell lines573
- Note cautions about bleeding: ask your doctor or pharmacist or see the Cautions section of our Aspirin and Other Non-steroidal Anti-inflammatory Drugs (NSAIDs) page
- Used in these programs and protocols:
    - Block program574
    - Chang strategies575

Bisphosphonates

- Modestly reduced risk of colorectal cancer576
- Note several side effects.
- Requires a prescription from a licensed physician

Metformin

- Reduced risk with use in some but not all analyses,577 including in those with type 2 diabetes578
- Decreased risk of colorectal adenoma recurrence579 and reduced aberrant crypt foci (a pre-cancerous condition) in patients at high risk of adenoma recurrence580
- Prevented metachronous (not concurrent) colorectal adenomas or polyps581
- Requires a prescription from a licensed physician
- Used in the Block program582

Nonsteroidal anti-inflammatory drugs (NSAIDs) other than aspirin (MedicineNet)

- General NSAIDs other than aspirin:
    - Reduced risk of colorectal cancer583 especially of distal colon cancer, at higher doses, in women and in Caucasians584
- Celecoxib and other COX-2 inhibitors:
    - Lower adenoma recurrence in those with a history of previous adenoma, but with increased risk of cardiovascular events585

    - Lower colorectal cancer risk in high-risk populations (those with familial adenomatous polyposis [FAP], Lynch syndrome or mutations that involve DNA repair pathways), but with increased risk of cardiovascular events586
    - Reduced number of colorectal polyps in young adults with familial adenomatous polyposis587
- Sulindac:
    - Decreased number of polyps and their diameter in patients with familial adenomatous polyposis (FAP)588
    - Lower colorectal cancer risk in high-risk populations (those with familial adenomatous polyposis [FAP], Lynch syndrome or mutations that involve pathways of DNA repair), but with increased risk of cardiovascular events589
    - Decreased risk when used with difluoromethylornithine (DFMO), without a significant increase in adverse events590
- Risks of serious side effects (especially gastrointestinal and cardiovascular) must be considered against potential benefits;.591 see Cautions on our Aspirin and Non-steroidal Anti-inflammatory Drugs page
- May require a prescription from a licensed physician

Thiazolidinediones (TZDs)
Examples include pioglitazone (Actos) and rosiglitazone (Avandia)

- Modestly reduced risk of colorectal cancer592
- Requires a prescription from a licensed physician

Group B: Limited clinical evidence of efficacy

May be used in integrative protocols and programs

Artesunate

- Reduced disease recurrence when used at the time of surgery in a small trial593
- Note cautions on our Artemisinin and Artesunate page.

Statins

- Reduced risk of colorectal cancer in large epidemiological studies, but not always in randomized controlled studies, case control and cohort studies, perhaps because of shorter timeframes and confounding conditions, or perhaps because of publication bias in epidemiological studies594
- Mixed evidence regarding reduced risk of recurrent, multiple or advanced adenomas or adenomatous polyps595
- Reduced risk for patients with diabetes or irritable bowel disease (IBD) with long-term use596
- Notable preclinical evidence: reduced colorectal cancer development in mice597
- Requires a prescription from a licensed physician

- Note cautions.
- Used in the Chang strategies598 in a "cocktail" treatment for preventing cancer occurrence as well as recurrence, especially for colon cancer

Optimizing Your Terrain

Creating an environment within your body that does not support cancer development, growth or spread

Cytokines, Inflammation and Outcomes

Cytokines are proteins with a complex relationship to your immune system and sleep cycles. If your circadian rhythm is disrupted by an external change in the light-dark cycle—such as by night-shift work or staying awake late at night—your immune cells produce a heightened inflammatory response driven in part by cytokine release.599

In patients with metastatic colorectal cancer, higher levels of inflammatory cytokines were linked to disrupted rest/activity circadian rhythms. Higher cytokine levels were associated with poorer response to chronochemotherapy (chemotherapy timed by circadian rhythms), poorer survival, increased fatigue and loss of appetite.600

Therapies that reduce inflammation and promote more typical sleep-activity rhythms may impact cytokine release and improve outcomes.

Natural Products

Garlic supplements, including aged garlic extract
The effects of garlic in your diet are discussed above in Eating Well.

- Increased immune function (the number and activity of natural killer cells) in those with advanced inoperable colon cancer.601
- Reduced blood coagulation602
- Modest reduction in blood pressure in patients with mild hypertension with a garlic powder preparation603
- Managed blood glucose604
- Caution regarding increased risk of colorectal cancer with use
- Used in the Block program605 for coagulation

Astragalus and other saponins

- Anti-inflammatory606
- Immune support or modulation607

- Antioxidant608

Combinations of therapies

- Couplet medicines (Astragalus membranaceus and Jiaozhen)
    - Anti-inflammatory609
- Daikenchuto (ginger, ginseng, and Zanthoxylum fruit)
    - Suppressed postoperative inflammation following surgery for colorectal cancer610
- Quxie Capsule (a combination of traditional Chinese medicine therapies):
    - Immune modulation611

Curcumin

- Anti-inflammatory and antioxidant,612 including greater elevation in enzymes and activity that reduce systemic oxidative stress in patients with solid tumors receiving standard chemotherapy regimens613
- Decreased serum levels of TNF-α, a protein that may boost immune response and may also cause death of some types of tumor cells614
- Effects on gene expression and signaling pathways615
- The Meriva formulation decreased oxidative stress and systemic inflammation in patients with solid tumors undergoing chemotherapy.616
- Normalized and diversified the colon microbiota, reducing inflammation in the colon and preventing colon cancer in mice617
- Used in these protocols and programs:
    - Alschuler & Gazella complementary approaches618
    - Block program619

Fermented wheat germ extract

- Favorably impacted immune response620 and enhanced immune activity in animal studies621

Ginger

- Antioxidant effects in preclinical studies622
- Anti-inflammatory effects in preclinical studies, with limited clinical evidence;623 . nanoparticles derived from edible ginger showed anti-inflammatory properties in animal studies.624
- Improved intestinal barrier function625
- Inhibits enzyme action and may impact the microbiome626
- Alters cell signaling pathways627
- Regulates genes that promote cell death (apoptosis)628
- Used in these programs and protocols to reduce inflammation:
    - Alschuler & Gazella complementary approaches629
    - Block program630

    - McKinney protocols631

L-glutamine, also known as glutamine

- Decreased inflammation among patients with prostate or rectal cancer receiving radiation therapy632 or combination radiation and chemotherapy633
- Improved nitrogen balance and boosted immune system response634
- An oral nutrition supplement enriched with carbohydrates, glutamine and antioxidants before surgery somewhat weakened but did not prevent peripheral insulin resistance following surgery.635
- Balanced glucose-insulin homeostasis and facilitated recovery in patients undergoing colon cancer resection.636
- Reduced the usual decrease in branched-chain amino acids (BCAA, a group of three essential amino acids) after surgery with glutamine-enriched total parenteral nutrition (TPN)637

Grape seed extract

- Supports healthy coagulation by inhibiting clotting processes that protect tumor cells and facilitate metastasis638
- Anti-inflammatory,639 including reduced inflammation in mice640
- Antioxidant641
- Used in the Block program642 for hypercoagulation (excessive blood clotting)

Green tea extracts/EGCG

The effects of drinking tea are discussed above in Eating Well.

- Antioxidant643
- Anti-inflammatory644
- Antimutagenic (counteracts the effects of mutagens, which cause genetic mutations) and anticarcinogenic645 including reduced instability in chromosomes in noncancerous colon cells646
- Inhibited VEGF (a substance made by cells that stimulates new blood vessel formation) and other growth factors647
- Reduced fasting blood glucose in some studies and meta-analyses,648 but not all649
- Used in these programs and protocols:
    - Alschuler & Gazella complementary approaches650 for inflammation, insulin function/blood sugar regulation and oxidation; used specifically with colorectal cancer
    - Block program651 for inflammation, insulin function/blood sugar regulation specifically with colorectal cancer
    - McKinney protocols652 for inflammation, insulin function/blood sugar regulation

L-carnosine

- Antioxidant and anti-inflammatory653

L-glycine

- Anti-inflammatory, immunomodulatory and protective of cells (cytoprotective)654

Omega-3 fatty acids

The effects of omega-3s in your diet are discussed above in Eating Well.

- Reduced inflammation,655 or improved anti-inflammatory markers656 including when accompanying anticancer treatment657 and in patients undergoing radical colorectal cancer resection658

Probiotics

- Improved immune response659
- Improved intestinal microbial environment660

Turkey tail mushrooms or extracts

- Inhibited processes that prevent the immune system from recognizing and responding to the cancer in people with gastrointestinal cancer661
- Positive immune impacts in patients with gastrointestinal cancer662

Vitamin C

- Low plasma AA concentration is associated with high levels of an inflammatory marker (C-reactive protein)663

Vitamin E supplements

- Improved immune activity in patients with advanced colorectal cancer664

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

Aspirin

- Anti-inflammatory665
- Significan cautions regarding gastrointestinal bleeding and other risks with use; see Cautions on our Aspirin and Non-steroidal Anti-inflammatory Drugs page
- Used in the Block program666 for inflammation

Bisphosphonates (Cancer Research UK) (Clodronate liposomes)

- Increased immune biomarkers in mice667
- Increased gut bacteria associated with reduced colorectal cancer risk in mice668

Cimetidine (Tagamet HB)

- Immune and immunomodulatory effects,669 including a more rapid return to pre-operative immune function after surgery670

- Reduced adhesion, a process that facilitates metastasis671
- Note cautions and drug interactions: ask your doctor or pharmacist.
- Used in these protocols and programs:
    - Block program672 for immunity
    - Lemole, Mehta & McKee protocols673 for immunomodulation

Copper chelation with tetrathiomolybdate (TM) and other substances

- Anti-inflammatory674
- Improved immune pathway response in animals675

Metformin

- Anti-inflammatory676
- Reduced blood glucose (glycemia);677 elevated levels are a risk factor for colorectal cancer678 and are associated with poorer survival in some reports679
- Requires a prescription from a licensed physician
- Used in these protocols and programs for glycemia
    - Block program680
    - McKinney protocols,681 with care to monitor vitamin B12 status

Nonsteroidal anti-inflammatory drugs (NSAIDs) other than aspirin

- Anti-inflammatory682
- Risks of serious side effects (especially gastrointestinal and cardiovascular) must be considered against potential benefits;.683 see Cautions on our Aspirin and Non-steroidal Anti-inflammatory Drugs page
- May require a prescription from a licensed physician

Rapamycin (sirolimus)

- Metabolic response with short-course radiotherapy in rectal cancer patients684
- Requires a prescription from a licensed physician

Statins

- Anti-inflammatory685
- Note cautions on our Statins page.
- Requires a prescription from a licensed physician
- Used in the Block program686 for inflammation

Other Therapies

Acupuncture and Electroacupuncture

- Electroacupuncture during laparoscopic radical rectectomy for rectal cancer decreased markers of inflammation after surgery.687

Short-term fasting

- Antioxidant and anti-inflammatory688
- Altered growth factors and metabolite levels, reducing the capability of cancer cells to adapt and survive;689 similar effects can be achieved with a fasting-mimicking diet (FMD)690
- Promoted cell self-clearing (autophagy); similar effects can be achieved with a fasting-mimicking diet (FMD)691

Your Microbiome and Colorectal Cancer

Antibiotic Use and Colorectal Cancer

Antibiotics can dramatically alter your microbiome. More frequent or oral antibiotic use was linked to a 17% increased risk of colon cancer but a reduced risk of rectal cancer (mostly among women) in a very large observational study.692 In a separate very large study, the increased risk was evident even with minimal use or with use 10 or more years prior to diagnosis, and risk was strongest with antibiotics with anti-anaerobic effects.693

"When asked about the difference between the apparent impact of antibiotic use on the risk of cancer in the colon when compared to the rectum, [senior author Cynthia] Sears commented, 'We think these differences highlight the differences in biology and likely the microbiome between these two cancer sites. Hence we hypothesize that antibiotics impact disease at these sites differently.'"694

We know that lifestyle factors and your gut microbiome interact to influence the development and progression of colorectal cancer. We are not yet clear on exactly how this plays out in people or what we can do to manipulate the microbiome favorably. We know that diet influences the microbial community in the gut. Researchers think the interaction between diet and gut microbiota influences colorectal cancer development by changing your metabolism and immune system.695 Evidence supports these assertions:

- A high-fat diet is bad news for gut health, as it produces secondary bile acids. These acids change the microbiome, resulting in increased oxidation and inflammation that damage colon cells.696
- Beneficial bacteria in the gut are needed to process and create essential nutrients by fermenting dietary fiber and producing butyrate. These microbial processes provide energy to colon cells and promote protective immune system effects. Adequate dietary fiber is thus essential for a healthy interplay between the gut microbiome, colon cells and immunity.697 Lower levels of butyrate-producing bacteria are associated with the presence of colorectal cancer.698
- Impacts of a healthy microbiome with colorectal cancer include these:699
- A healthy gut microbiome appears to support the anticancer action of the chemotherapy drug oxaliplatin.

- Bacteria in the genus Bifidobacterium are crucial to optimizing the anticancer action of ligand 1 drugs (PD 1 checkpoint inhibitors), which activate the immune system to attack tumors.
- Gut microbes can prevent reactivation of drug metabolites that can damage the intestines and cause diarrhea related to drugs such as camptothecin.
- Microbial species in the intestines can impact inflammation.

People with colorectal cancer have less diverse gut bacteria, with reduced levels of Bifidobacterium, Clostridium, Faecalibacterium and Roseburia, for instance. Harmful species including Escherichia coli, E. faecalis, F. nucleatum, and Streptococcus gallolyticus also tend to be present in colorectal cancer patients.700 For example, enterotoxigenic Bacteroides fragilis [ETBF], which produces toxins in the digestive tract, is associated with a greater number of early-stage carcinogenic lesions and increased risk of colorectal cancer.701

Probiotics, Prebiotics and Synbiotics

Probiotics are living microorganisms (bacteria and some yeasts) that can provide health benefits that go beyond basic nutrition, such as supporting gut and immune health and keeping the gut microbiota in balance. Examples of probiotic foods are yogurt, kefir, sauerkraut, tempeh and kimchi. Probiotics must be consumed in sufficient numbers to be effective.

Prebiotics are dietary fibers that feed the friendly bacteria in your gut. Most prebiotics are soluble fiber substances like inulin, found in foods like bananas, onions, jerusalem artichokes, jicama, garlic and others, plus chicory root. Your helpful bacteria turn inulin and other fibers into energy for the colon cells and create protective immunity. Inulin is increasingly being added to a number of processed foods and probiotic supplements.

Synbiotics contain prebiotics and probiotics together.

Use of pre- and probiotics can reduce some symptoms and side effects of cancer treatments and can improve the gut microbiome and impact inflammation as described above.

Surgery and Colorectal Cancer

Key Points: Surgery and Colorectal Cancer

- Surgery as a treatment for colorectal cancer can greatly improve the prognosis but can involve several complications that can reduce CRC survival and increase the risk of recurrence.
- Some factors that increase the risk of surgical complications are under the control or influence of the surgical team and/or the patient. Others, such as age, gender or prior abdominal surgery, are not.
- Numerous negative consequences of surgical complications are possible, so a proactive approach to prevent them is important.

- Prehabilitation and/or enhanced recovery after surgery (ERAS) programs and interventions are designed to prevent or lessen the complications of surgery.

Colorectal cancer treatment often includes surgery. The surgery may provide long-term benefit regarding cancer outcomes, but risks and complications are also relatively commonplace. We provide a brief overview of issues and integrative approaches surrounding colorectal cancer surgery. General information about surgery with cancer is available on our Integrative Approaches to Surgery page.
Clinical Practice Guidelines
For Healthcare Professionals: Enhanced Recovery after Surgery (ERAS)

ERAS is an approach focusing on counselling before surgery, optimizing nutrition, standardizing approaches to pain relief and getting you (the patient) moving and on your feet following surgery. It draws from several modalities, such as nutrition, medication, movement and counseling.702

In patients undergoing extensive pelvic dissection, ERAS can improve recovery, reduce the rate of complications and reduce the length of hospital stay following surgery. ERAS also provides early warning for later complications.703 See a discussion of ERAS protocols and outcomes: Enhanced recovery after rectal surgery: what we have learned so far and Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) group recommendations.

ERAS includes returning to eating by mouth after surgery as soon as practical, with several benefits:704

- Prevent your body from getting energy from body tissue, such as muscles, leading to wasting (cachexia)
- Improve your immune function and reduce your systemic inflammatory response
- Reduce the permeability of your intestinal lining ("leaky gut"), reducing movement of bacteria from your intestinal tract to other areas of your body

Being informed and engaged is key to optimal nutrition following surgery.

Optimal nutrition also improves your body terrain factors:

- Nutritional supplements containing glutamine, arginine, omega-3 fatty acids and ribonucleic acid can reduce inflammation and improve your immune response.705
- Including amino acids in low-energy tube feeding (parenteral nutrition) prevented protein loss after gastrointestinal surgery. The benefit was through a smaller impact on nitrogen balance and increased protein metabolism.706

Guidelines for patients from the Enhanced Recovery After Surgery (ERAS®) Society:707

- Recommendations before hospital admission:
    - Stop smoking at least four weeks before surgery to reduce problems with breathing and wound healing
    - Engage in a prehab activity program (see below) to promote quicker recovery of function and fewer complications, especially if you are less fit
- Recommendations before surgery:
    - Avoid sedatives such as benzodiazepines if possible; taper a withdrawal if needed.708 Also, see Integrative Approaches and Surgery for a list of supplements to stop taking before surgery.
- Recommendations following surgery:
    - When you are allowed to eat, choose healthier foods from the menu. See Integrative Approaches and Surgery for examples of healthy eating when recovering from surgery.
    - If prescribed, use oral nutritional supplements from the day of surgery or as directed by your doctor.
    - Move as much as comfortable, including getting on your feet as soon as you can.

The American Society of Colon and Rectal Surgeons and Society of American Gastrointestinal and Endoscopic Surgeons provide guidelines for the surgical team: Clinical practice guidelines for enhanced recovery after colon and rectal surgery from the American Society of Colon and Rectal Surgeons and Society of American Gastrointestinal and Endoscopic Surgeons.709

Prehab and Surgical Outcomes

Prehabilitation (prehab), “the process of enhancing physical fitness before an operation to enable the patient to withstand the stress of surgery,” can reduce several risk factors for surgical complications, including malnutrition, anxiety and depression, and may also help to manage uncontrolled conditions or comorbidities, including glycemia, diabetes, hypertension and anemia.710

Prehab may include exercise training, counseling and oversight regarding nutrition, and strategies for coping with anxiety and distress. See information about nutrition in the Nutrition and Surgery section of our Integrative Approaches and Surgery page. Information about managing anxiety before surgery is in the Managing Anxiety before Surgery section of that page.

Nutritional guidelines for patients undergoing surgery for colorectal cancer:711

- Meet your energy requirements: One in four colorectal cancer patients has elevated metabolism (hypermetabolism), even those with good physical status. Hypermetabolism is linked to negative energy balance, weight loss, systemic inflammation and decreased ability to function in daily activities. Common formulas for determining energy requirements are not accurate in this situation. Work with your care team to use indirect

calorimetry with adjustments for additional exercise and physical activity, which is more helpful.
    - A high-protein diet, modified for those with kidney disease
    - Meals should be balanced in this ratio
    - Two servings of starches
    - One of high-protein sources
    - Two of vegetables
- Follow basic healthy dietary suggestions before surgery, following further recommendations from your healthcare providers for your specific condition.

Surgical Factors Associated with Increased Recurrence Risk

Even though surgery is a routine treatment for solid tumors, surgery itself can promote the development of metastasis by releasing tumor cells into circulation, suppressing important immune defenses such as your cellular immune system and and promoting the development of blood vessels to supply tumors (angiogenesis).712
Type of Surgery: Open or Laparoscopic

The type of surgery—whether open surgery or laparoscopic surgery—has a great impact on the resulting inflammation—greater than the choice of anesthetic and pain management techniques (epidural versus intravenous analgesia).

Surgery initiates a local inflammatory response, starting with the incision, which the body interprets as a wound. Circulating tumor cells are drawn to wounds, infection sites and tissue trauma, setting up a microenvironment in distant organs conducive to the survival and growth of tumor cells. This is called a premetastatic niche. In addition, systemic inflammation—such as in metabolic syndrome, chronic stress response or chronic insomnia—also creates a microenvironment supportive to tumors.

The more extensive the surgery, the greater your inflammatory response. More extensive surgery could tip the stress-inflammatory response in the direction of metastasis even when the primary tumor is successfully removed. The wound-healing process can release immune system chemicals known to promote tumor growth.713 In fact, abdominal/pelvic surgery is associated with metastasis across the peritoneal cavity.714

It would seem that laparoscopic surgery reduces this potential. However, a small study in Europe found no significant difference in recurrence or survival between open and laparoscopic surgery in patients undergoing surgery with chemo-irradiated rectum tumors. The length of the follow-up period was not specified.715 Much more evidence is needed.

Surgical Conditions

Mild low body temperature (hypothermia) worsens the suppression of your immune response from abdominal surgery.716 Hypothermia may impair your immune system's ability to stop infection and kill cancer cells. Maintaining your body temperature during surgery will reduce your risk of immune suppression.

Use of blood transfusion products can cause suppression of your immune response and increase your risk of recurrence.717 Blood transfusion using your own blood (autologous transfusion) may reduce your risk of recurrence.718
Patient Condition at the Time of Surgery

Your stress level and other characteristics around the time of surgery can affect your immune system and may increase your risk of recurrence:

- Your surgical stress response subdues your immune system's ability to stop infection and kill cancer cells, increasing the likelihood that cancer cells will travel and lead to metastasis.719
- Your stress level can act to suppress your immune system separate from your surgical stress response. Higher levels of stress are linked to greater suppression of the immune system after surgery, including natural killer cells and the response of antitumor T cells.720
- Your physical condition: lower fitness for surgery—such as measured by a high Physiological and Operative Severity Score for the Enumeration of Mortality and Morbidity (POSSUM)—and a high systemic inflammatory response before surgery predict early disease recurrence after a potentially curative resection for colorectal cancer.721
- Your mood (anxiety and/or depression) can depress your immunity.722

Reducing Factors around the Time of Surgery that Increase Recurrence Risk

Delaying Surgery and Survival

Delaying surgery may lead to poorer survival, according to a systematic review. Conclusions from the review:723

- With primarily resected colon cancer, delays of more than 30 to 40 days are associated with lower survival.
- With rectal cancer, performing surgery more than seven to eight weeks following neoadjuvant therapy (therapy prior to surgery) was associated with decreased survival.

Combined use of the beta blocker propranolol and the anti-inflammatory etodolac for five days before surgery has been used safely to reduce metastases and mortality. However, this

combination may not be safe in patients with asthma, cardiovascular disease, diabetes, bleeding risk, GI ulcers or low blood pressure.724

Taking precautions to prevent blood clots, neutrophil extracellular traps (NETs) and low oxygen levels (hypoxia) may reduce recurrence after surgery.725

Surgical Complications and Infections

Surgical Complications

Colorectal cancer surgery can involve several possible complications:726

During surgery:

- Bleeding
- Bowel injury
- Lesions in ureters
- Bladder injuries due to adhesions, problems with the anastomosis (the place where colon sections are joined after a section is removed) and due to surgeon's inexperience

After surgery:

- Surgical site infection
- Leakage of the anastomosis
- Bowel or intestinal blockage or paralysis (ileus)
- Bleeding
- Pneumonia
- Urinary tract infection
- Fistula, an abnormal passageway between body parts, for example from the colon to another organ such as the bladder

Infections and complications of surgery not only make recovery more difficult, they may impact your cancer outcomes and even your survival (see sidebar).727

Colorectal surgery is invasive and disrupts the equilibrium of your gut microbiome—the microbes in your gut. A microbial imbalance can impair the function of your local immune response, promote systemic inflammation, and potentially lead to infection following surgery.728 Perhaps due to the large number of bacteria present in the colon and rectum, the number of surgical site infections in patients undergoing colorectal surgery is high—up to 26 percent.

Complications can reduce survival through several routes:

- Infection increases inflammation, which is associated with increased risk of local recurrence and cancer spread.
- Complications can delay chemotherapy treatment, which may lead to poorer outcomes.729
- Complications of surgery—especially anastomotic leaks (where colon sections are joined)—can lead to longer hospital stays and increased risk for hospital-acquired complications, as well as increased risks of readmission, of reoperations and of mortality.730
- Complications following surgery that decrease survival and increase recurrence risk:731
    - Anastomotic leakage
    - Pneumonia
    - Bowel obstruction/ileus
    - Infection at the surgical site
    - Postoperative bleeding
    - Urinary tract infection
    - Fistula (an abnormal connection between two body parts)

Factors Increasing Risk of Infection and Other Complications

Can Be Influenced or Controlled

- Obesity[a]
- Smoking[a]
- Nutritional status[b]
- Uncontrolled conditions or comorbidities, including glycemia, diabetes, hypertension and anemia[a]
- Type of surgery, whether open or laparoscopic, plus how complications caused by surgery and treatment (such as nicking the bladder) are handled, choice of instruments, management of blood loss in surgery, prophylactic draining, creating a protective stoma and operating time
- Choice of pain control and diet following surgery
- Choice of surgeon and hospital/clinic[c]
- Anxiety and depression present before surgeryd
- Inflammation or compromised immunity[a]
- Chemoradiotherapy before surgery[e]
- Mechanical bowel preparation before surgery[g]
- Low muscle mass or density before surgery[h]

Cannot Be Influenced

- Age (65 or older)[a]
- Gender

- Prior abdominal surgery
- Adhesions (scar-like tissues that adhere together)

Factors Not Increasing Risk

- Radiotherapy before surgery[e]

a. Obesity, smoking, glycemia, hypertension, diabetes, anemia-compromised immunity or inflammation, and patient age 65 or older are each linked to increased wound complications following surgery.732 In elective surgery in overweight patients, weight loss before surgery is recommended, as is correction of anemia with iron, vitamin B12 and folate supplementation as needed, such as for pernicious anemia.733
b. Malnutrition is linked to a greater chance of surgical complications, longer hospital stay, less tolerance of other cancer treatments, higher risk of death and higher health-care costs.734
c. Surgeons with more experience as well as hospitals with higher numbers of colorectal surgery patients are associated with fewer complications and, in some studies, lower risk of recurrence and higher survival.735
d. Anxiety and depression before surgery negatively affect wound healing, your risks of infection and a longer hospital stay, and your ability to adhere to your medical treatment plan.736
e. A 2016 meta-analysis found that radiation therapy before radical rectal cancer surgery didn't increase risk of wound complications.737 However, some evidence shows increased risk of infection and other complications such as anastomotic leakage with chemoradiotherapy before surgery.738
f. Men are at higher risk than women of anastomotic leaks with rectal cancer surgery.739
g. The current standard to reduce infection risk is called mechanical bowel preparation (MBP, giving oral medicine to clear feces from the intestines) plus prophylactic antibiotics. Some research has suggested that MBP doesn't improve infection outcomes and may cause greater harm because it is often poorly tolerated.740
h. Low skeletal muscle mass and density were associated with longer hospital stays and higher risks of postsurgical complications, and both short-term and long-term mortality.741

Preventing Surgical Complications

Anastomotic Leaks

Anastomotic leaks—occurring at the place where colon sections are joined after a section is removed— can lead to other problems such as longer hospital stays; higher risks of readmission,

reoperations or mortality; and a worse quality of life. Patients who have anastomotic leaks following cancer operations also have a higher risk of distant recurrence and long delays in receiving indicated adjuvant (supplemental) chemotherapy.

Recognized or proposed risk factors include these (also see the discussion below of pain control and surgical outcomes):742

- Male
- Age greater than 60 years
- Smoker
- Malnourished and/or diabetic patients
- Open surgery (vs laparoscopic)
- Prolonged operating time
- Emergency surgery
- Rectal surgery
- Lack of a protective stoma in rectal surgery
- Coexisting (comorbid) conditions

Interventions for the surgical team to reduce the incidence of anastomotic leaks:743

- Use surgical techniques that minimize surgery time
- Reduce inadequate blood supply to tissues (tissue ischemia)
- Use staples to join the ends
- Provide five to seven days of nutritional supplementation to boost immune function for malnourished patients before surgery: a high-protein nutritional supplement with the addition of immune-enhancing components such as glutamine, arginine, omega-3 fatty acids, and ribonucleic acids
- Avoid early operations (less than four weeks) following chemotherapy
- Limit drugs that constrict blood vessels (isoproterenol, phenylephrine, norepinephrine, epinephrine)
- Use an oral antibiotic preparation
- Use goal-directed fluid management
- Limit steroid use

Interventions for patients:

- Stop smoking in the period surrounding surgery

Reducing the risk of complications: what you and your surgeon can do

What You Can Do

- First, find out how much time you can take before surgery to develop a plan and prepare for surgery.
- Preparing your body

- Discuss which risk factors you can improve before surgery and come up with a plan of actions to take. Actions may include controlling hypertension, stress, hyperglycemia and other conditions, or stopping smoking
- Consider incorporating stress management practices in the weeks leading up to surgery. Many patients find imagery practices specific to preparing for surgery to be helpful. See Managing Stress, Stress, Mind-Body Approaches and Guided Imagery.
- In addition to effective stress management practices, use emotional support, counseling and pre-surgery medication as appropriate to help reduce preoperative psychological stress.
- If you typically clean an animal litter box or bird cage, find someone else to clean it before and for several weeks after your surgery.
- Optimizing your surgical context:
- Check postoperative infection rates for the hospital where your surgery will be performed at Medicare.gov—Hospital Compare. While individual surgeon complication rates are available for many types of surgery, they are not published for breast surgery. Having said that, infection rates tend to be higher on average with less-experienced surgeons (a pretty good rule of thumb for having good experience is to consider surgeons who have done at least four per month of your specific type of surgery for five years).
- Inform your surgical team of any supplements, herbs or other therapies you're using prior to surgery.
- If you have financial or social barriers to good pre- and postsurgical care, ask to be referred to an oncology social worker or oncology navigator for assistance.
- Schedule your surgery as an ambulatory procedure rather than as an inpatient hospital stay, if possible.
- Discuss your options for anesthesia, post-surgical pain control (see more about ERAS protocols above) and the steps in the column at right with your surgical team at the pre-op visit.
- Immediately before surgery:
- Avoid presurgical dehydration.
- See if you can postpone surgery if you develop a cold, flu, pneumonia or other infection shortly before scheduled surgery.
- After surgery
- Before leaving the hospital, be sure you (and anyone who will be assisting you at home) fully understand and follow all wound care instructions carefully. Call your physician immediately if you show any signs of infection—an increase of redness, swelling, pain or discharge from your wound.
- Avoid contact with soil for two or more weeks after surgery.
- Consult an integrative physician or licensed naturopath (preferably one who is certified in oncology) to recommend approaches to maintain healthy immune function to improve your wound healing and reduce your risk of infection.

- In the weeks following your surgery, if you need a medical procedure that may introduce bacteria to the body, check with your surgeon about using antibiotics to prevent infection.

What Your Surgeon Can Do

- Assess all choices and optimize risk factors, including patient characteristics and their status of adjuvant therapy, such as radiotherapy and chemotherapy.
- Because half of infections occur more than 30 days after a procedure, implement a plan for follow-up care, including appointments and phone calls.
- Reduce suppression of the immune system induced by surgery and anesthesia:744
- Use regional anesthesia and IV propofol as the primary anesthetic when possible
- Provide adequate pain control throughout the surgical experience while minimizing the use of opioids such as morphine, oxycodone or codeine.
- Avoid opioids during or after surgery by using an intravenous propacetamol and anti-inflammatories such as ketorolac while in the hospital and then using oral anti-inflammatories such as ibuprofen or naproxen after discharge.
- Avoid hypothermia by maintaining core body temperature devices such as fluid warmers and external body warmers.
- Remove catheters and drains as soon as possible.
- Use antibiotic prophylaxis.

HA/CMC film adhesion barrier: A hyaluronic acid/carboxymethylcellulose (HA/CMC) film adhesion barrier can reduce adhesion formation, but a multicenter study found its use increased the risk of total adverse events and serious adverse events including excess body heat (hyperthermia), abscess in the pelvic area or incision site, urinary tract infection, urinary retention and ileus (bowel or intestinal blockage or paralysis).745

Infection and Treatment Outcomes

Infection may delay cancer treatments such as chemotherapy or radiation, leading to less effective treatment and worse outcomes, including recurrence.746

Some evidence shows that radiochemotherapy before surgery for rectal cancer may increase risk of infection and other complications such as anastomotic leakage.747 However, a 2016 meta-analysis found that radiation therapy alone before radical rectal cancer surgery didn't increase risk of short-term wound complications,748 although side effects and a decreased quality of life may prolong recovery from surgery.749 Because treatment decreases the risk of local recurrence (but without changing cancer survival outcomes or your risk of distant metastasis), both risks and benefits need to be considered with your oncology team.750

Preventing Infection

Laparoscopic surgery: Fewer wound-related complications, including infections and fever, were seen with laparoscopic surgery compared to open surgery in patients with chemo-irradiated rectum tumors. The need for transfusion was also lower with laparoscopic surgery.751

Taurolidine: Non-metastatic colon cancer patients undergoing surgery receiving taurolidine (ScienceDirect) showed reduced inflammation, lower risk of surgical site infection and possibly lower rates of recurrence two years after surgery.752

Antibiotics: Systemic ultra-short and short-term antibiotic preventive treatment (prophylaxis) before and during surgery reduces the risk of postsurgical infection. Some studies suggest giving both oral and intravenous (IV) antibiotics for greater effect. Oral, non-absorbable antibiotics may reduce risk not only of surgical site infection but also of anastomotic leak.753

However, prolonged antibiotic use, such as what might be required if an infection or anastomotic leak develops following surgery, may impair the function of your immune and neuroendocrine systems, increasing your risk of future infection and/or recurrence. Minimizing your risk of infection and thus reducing the need for prolonged use of antibiotics is important.

Prebiotics or probiotics: Some studies conclude that prebiotic or probiotic use around the time of surgery may reduce infections following surgery and help maintain the intestinal mucosal barrier, while other studies have shown no effect.754

Early mobilization—patient movement as much and as often as tolerable, including getting out of bed and walking—reduces the risk of pneumonia as well as surgery complications not related to infection, such as deep vein thrombosis (DVT), muscle loss and insulin resistance.755

A 2018 review concluded that these measures reduce surgical site infection after rectal surgery:756

- Antibiotic prophylaxis (see below)
- Preventing low body temperature (hypothermia)
- Hair removal
- Preventing high levels of blood glucose (hyperglycemia)

Other proposed interventions:

- No fluid overload
- Skin preparation with chlorhexidine
- Double gloving or change of gloves and gowns before closing the fascia
- Lavage of subcutaneous tissue
- Silver dressing

Actions if You Develop an Infection

- Report symptoms of infection immediately to your surgeon and begin treatment promptly. If antibiotics are prescribed, take as directed.
- Eat well to maintain a healthy nutritional state. Consider consulting a board-certified oncology dietician for specific dietary recommendations.
- If antibiotics are prescribed, eat well and follow other practices to restore a healthy microorganism balance. See Eating Well, Mediterranean Diet and Your Microbiome.
- Consider consulting an integrative oncology specialist about additional measures to clear infection, help wound healing, control inflammation and minimize tissue scarring (fibrosis) from surgical wounds and/or from radiation therapy.

Pain Control

Sufficient pain control following surgery is essential to improve the quality of convalescence and speed up recovery.757 However, pain control methods vary considerably in their impact on surgery and cancer outcomes. Wise use of therapies to manage pain is extremely important to optimize both surgical and cancer outcomes.

Effectiveness of Pain Control Approaches

Drug-based Pain Management

- Opioid-based intravenous patient controlled analgesia: Compared to epidural analgesia in laparoscopic surgery, opioid-based intravenous patient-controlled analgesia (IV PCA) using fentanyl showed comparable pain control, faster return of bowel function, fewer overall complications, and shorter hospital stays, plus less need of drugs to maintain blood pressure.758
- Continuous surgical wound infiltration with local anesthetics used after laparoscopic colorectal surgery reported similar pain control efficacy as opioid-based IV PCA (above) in at least some patients.759
- Thoracic epidural analgesia (TEA) was more effective than IV-PCA (see above) after open colorectal cancer surgery, with a better bowel function, dietary intake, patient satisfaction and early mobilization in a small trial.760
- Quadratus lumborum block (QLB) was more effective analgesia following surgery than the transversus abdominis plane block.761
- Transabdominus plane (TAP) blocks for anesthesia as part of an enhanced recovery program with laparoscopic and robotic-assisted colorectal cancer surgery reduced the length of hospital stay, use of narcotics following surgery and the time until the patient was walking and resumed bowel function.762
- A small pilot study investigated a multimodal pain management protocol (administered after induction anesthesia) in patients undergoing a laparoscopic resection of colorectal cancer. The protocol used a bilateral TAP block and local abdominal cavity infiltration with long-acting local anesthetic liposomal bupivacaine. Patients on this protocol

required fewer opioids during surgery, had shorter stays in the post-anesthesia care unit (PACU), less pain following surgery, less use of narcotics and a shorter hospital stay compared to a group that received no block or local wound infiltration.763

- The COX 2 selective inhibitor parecoxib—a non-steroidal anti-inflammatory drug—before surgical incision (compared to after incision) in colorectal cancer surgery reduced morphine use following surgery without affecting morphine-related side effects. Use before incision also reduced markers of inflammation.764

Non-drug Pain Management

- Acupuncture reduced the need for general anesthesia during rectal cancer surgery.765
- Transcutaneous electrical acupoint stimulation combined with transversus abdominis plane block (above): patients reported lower pain and lower opioid use following surgery than those receiving neither therapy.766

Impact of Pain Control Methods on Surgical Outcomes

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

Use of non-steroidal anti-inflammatory drugs (NSAIDs), and especially non-selective NSAIDs, following surgery may increase your risk of anastomotic leakage. Non-selective NSAIDs include diclofenac, diflunisal, etodolac, fenoprofen, flurbiprofen, ibuprofen, indomethacin, and ketoprofen.767 Diclofenac or celecoxib use was especially related to increased risk, as were higher doses of NSAIDs and starting use less than 48 hours after surgery.768

Acupuncture and Electroacupuncture

Use of acupuncture showed these benefits:

- Reduced time to first bowel sounds, first flatus and first defecation following surgery for colorectal cancer769
- Shorter fasting and time to peritoneal drainage tube withdrawal770
- Shorter hospital stay, shorter time to first flatus and shorter time to defecation among patients receiving both acupuncture and simo decoction (a traditional Chinese medicine) for five days following colorectal cancer resection771

Electroacupuncture impacts:

- Following laparoscopic surgery:
- Reduced duration of inability of the intestines to contract normally, which can lead to intestinal blockage blockage (ileus)772
- Reduced time to start walking (mobility)773
- Reduced use of pain relievers following laparoscopic surgery for colorectal cancer774

- Quicker recovery of gastrointestinal function with electroacupunture administered three times: one day and 30 minutes before surgery and one day after surgery; no improvement was reported with one or two electroacupuncture administrations775

Transcutaneous electrical acupoint stimulation (TEAS) impacts:

- Reduced inflammation after laparoscopic radical surgery for colon cancer776
- A trend toward less nausea and vomiting, shorter time to first flatus and oral feeding time following surgery when combined with transversus abdominis plane block compared to those receiving neither therapy777

Movement

A behavioral intervention—moving as soon as possible after surgery—reduced discomfort and the length of stay in the hospital.778

Opioids, Sedatives and Antidepressants

Adults undergoing colorectal resection who had used opioids, sedatives or antidepressants before surgery had higher rates of these outcomes compared to non-users:

- Ostomy creation
- Contaminated wound classification
- Prolonged operation time
- Transfusion following surgery
- Intra-abdominal infection
- Respiratory failure
- Longer hospital stays
- Increased 30-day morbidity and mortality

These patients also had lower fitness scores and more respiratory health issues than other patients.779

Impact of Pain Control Methods on Cancer Outcomes

Some approaches to managing pain may increase risks of suppressing your immune system and of cancer growth or recurrence.

Increased Risk of Immune Suppression and Possible Cancer Growth, Recurrence or Metastasis

General anesthesia: A small study of patients undergoing elective orthopedic surgery found a significant decrease of immune function using general anesthesia with fentanyl, thiopental and isoflurane.780

Regional anesthesia is favorable to general anesthesia—or even in addition to general anesthesia—for reducing inflammation, recurrence and metastasis in preliminary evidence.781

Volatile anesthetics: halothane, isoflurane, desflurane, and sevoflurane are volatile inhaled anesthetics that suppress the immune system and play a role in promoting cancer growth, perhaps through several pathways.782

Mixed Results

Opioids: The relationship of opioid drugs and cancer outcomes is difficult to separate from the effects of pain. Some evidence shows that opioid drugs—including morphine and tramadol—suppress immune responses and can promote tumor progression. However, cell studies have found that morphine both promoted and reduced processes of cell death (apoptosis). A 2014 review concluded that "further work is required to elucidate the possible impacts of morphine in cancer patients."783

Preliminary evidence shows that some opioids may be used for short periods without increasing risk of cancer mortality:

- A study found no differences in overall survival or disease-free survival at five years when comparing outcomes of using epidural, spinal block, or a morphine patient-controlled analgesia (PCA) for primary pain relief following surgery.784
- A small study compared the opioid fentanyl used as intravenous patient-controlled analgesia (IV PCA) to a regimen of local anesthetic wound infiltration-based analgesic and tramadol. "Rescue" analgesics were used: pethidine for the opioid group and ketorolac or propacetamol for the group receiving local anesthetic. The two approaches were comparable regarding immune function (natural killer cell cytotoxicity) and complications following surgery and recurrence or metastasis within one year after surgery.785
- Tramadol shows protective effects on immune function and reduced risks of recurrence and metastasis.786
- One study found use of opioids vs. use of local anesthetic did not affect cancer recurrence or metastasis for one year following surgery.787

Given that opioids may disrupt immune responses and function, preventing immune disruption may be warranted with use.

- Pretreatment with immunotherapy such as interferon may reduce some of the negative effects of opioids on your immune response, as suggested in animal studies.788
- If opioids are indicated, lower doses may disrupt your immune system function less than larger doses.789
- Substituting epidural analgesia for postoperative opioids may also improve outcomes.790

Treating pain after surgery with opioids hinders recurrence, even though opioids promote metastasis.791 A 2018 review of studies concludes “there is no conclusive evidence to avoid the use of opioids with the goal of reducing the risk of recurrence in colorectal cancer.”792

No Increased Risk or Reduced Risk

Non-steroidal anti-inflammatory drugs (NSAIDs)

- Use of NSAIDs at the time of surgery was associated with a reduced risk of cancer recurrence after resection for colorectal cancer. No effect was found on five-year mortality or disease-free survival.793 This benefit needs to be balanced with evidence of two increased risks with NSAID use:
- Risk for anastomotic leakage (see sidebar)
- Use of celecoxib (Celebrex) or indomethacin three days before surgery increased tumor infiltration, which could reduce cancer survival following tumor resection.794
- Aspirin use during chemoradiation therapy for rectal cancer before surgery was linked to better progression-free and overall survival.795
- One review found that NSAIDs may decrease tumor growth, with a link to longer recurrence-free survival. Effects for non-selective NSAIDs (aspirin, diclofenac, ibuprofen, naproxen and others) were influenced by the timing and dosage of use.796 Another study found that selective NSAIDs (Celebrex/celecoxib and Mobic/meloxicam) have protective effects on immune function and reduce recurrence and metastasis risk.797
- Ketorolac use before surgery in animals prevented both inflammation and “surgery-induced dormancy escape,” a process that can lead to tumor growth and metastasis.798
- Use of aspirin after surgery is associated with decreased risk of recurrence and death in colorectal cancer.799

Recovery and Remission Maintenance

Improving your body terrain can make your body less susceptible to infection, quicker to heal wounds and/or less favorable to cancer.

Survivorship

When you have finished treatment, your cancer treatment team should develop a survivorship plan with you, including these components to help you recover and prevent recurrence:

- Instructions and a schedule for follow-up visits
- Testing
- Guidance on lifestyle and other self-care practices

Post-Treatment Monitoring

The type of testing and monitoring used to assess your response to treatment and detect recurrence will depend on your specific cancer, treatment and risk for recurrence. A valid and reliable test to detect colorectal cancer recurrence early is still needed.

You and your medical team need to find balance with monitoring for colorectal cancer recurrence. Talk with your oncologist about your risk of recurrence and what type and frequency of monitoring is best for you:

- Have we done everything we know to do to treat the cancer?
- What type and frequency of monitoring is best for me?
- What are the monitoring tests and tools available?

The standard monitoring tests are typically are of two types:

- Radiographic scans (such as CAT scans) which involve the risks of significant radiation exposures. The more scans, the higher the risks.
- Measuring CEA (carcinoembryonic antigen) and Ca 19-9 in the blood. Unfortunately, these biomarkers are not good at detecting recurrence.

Neither scans nor tests such as CEA give genetic information about the intrinsic characteristics of each tumor.800

Potential Upcoming Diagnostic Tests

Talk with your doctor about whether one of these new biomarker tests is available for you. Some integrative oncologists are using these new biomarker tests already, but these tests have not been recognized by conventional oncology as a standard in clinical practice.

ctDNA Testing

Blood tests measuring circulating tumor DNA (ctDNA) have generated a lot of excitement and could be a new way to guide treatment decisions or as a trigger to look for residual disease or recurrence. These tests look for biomarkers of cancer recurrence, progression and resistance to therapy. Many potentially useful ctDNA markers are available. A 2019 review found ctDNA tests to be a sensitive and reliable measure of tumor burden.801 The American Society of Clinical Oncology—the main oncology society in the US—considers ctDNA testing promising, but stronger research is needed before it can be recommended for routine use in cancer care.

Measuring Circulating Tumor Cells (CTCs)

Measuring circulating tumor cells (CTCs) in the blood is another test under research and development.802 CTCs are cancer cells that break away from primary or metastatic tumors and enter the bloodstream; they are considered forerunners of metastasis. A 2019 study found that detecting CTCs with a fluid assisted separation technique (FAST) was promising as an early

diagnosis tool and biomarker for prognosis in colorectal cancer patients.803 These reviews suggest that CTCs may assist your healthcare team in these tasks:

- Predict survival
- Monitor your response/resistance to treatment
- Assess minimal residual disease
- Find and assess distant metastasis
- Customize therapies in some cases

Even though many difficulties related to CTC testing remain—limiting its use in managing colorectal cancer—reviewers think that their clinical use in colorectal cancer is not far off.804

For Health Professionals

Surveillance Schedule

Recommended schedule of surveillance for colon and rectal cancer (AJCC stage I (at increased risk for recurrence[a]), stage II, stage III, and stage IV (when isolated metastases are resected for cure)10

Colon

- Office visit and CEA every 3 to 6 months for 2 years, then every 6 months until 5 years
- CT chest/abdomen/pelvis[c] annually for 5 years[d]
- Colonoscopy 1 year after preoperative colonoscopy (or 3 to 6 months after surgery if colon not preoperatively “cleared")[e]

Rectum[b]

- Office visit and CEA every 3 to 6 months for 2 years, then every 6 months until 5 years
- CT chest/abdomen/pelvis annually for 5 years[d]
- Colonoscopy 1 year after preoperative colonoscopy (or 3 to 6 months after surgery if colon not preoperatively "cleared")[e]
- Proctoscopy (+/-ERUS) every 6 to 12 months[f] for patients who underwent resection with anastomosis or every 6 months for patients undergoing local excision for 3 to 5 years

Notes and Definitions

AJCC = American Joint Committee on Cancer
ERUS = endorectal ultrasound
LN = lymph node
Nx = nodal
s/p = status post

a. High risk of recurrence is defined by the treating provider. High-risk factors may include margin positivity (≤ 1 mm), Nx status (rectal cancer s/p local excision, higher-risk malignant polyps that do not undergo radical surgery, inadequate LN sampling), lymphovascular invasion, poorly differentiated tumors (grade 3 or 4), and T2 disease.
b. For patients who receive neoadjuvant therapy, these guidelines refer to clinical rather than pathologic stage.
c. PET-CT is not typically recommended, although PET-CT or MRI might be considered for imaging in a patient with contraindication to intravenous-contrast-enhanced CT scanning or to follow-up abnormalities seen on CT scans.
d. More frequent imaging may be considered for patients at particularly high risk for recurrence, including those with N2 disease, previous liver resection for metastasis, etc.
e. Further colonoscopy frequency depends on the results of the 1-year colonoscopy, with repeat examination in 3 years for patients without adenomas and 1 year for patients with adenomas. Annual colonoscopy is generally recommended for patients with confirmed or suspected familial cancer syndromes that have not undergone total proctocolectomy.
f. Patients at higher risk for local recurrence may be considered for the more frequent intervals, and for ERUS in addition to proctoscopy. Higher-risk patients may include those with poorer-risk tumors (eg, T2 or poor differentiation) who underwent local excision, those with positive margins (<1 mm), and those with T4 or N2 rectal cancers.

Authors

Laura Pole, RN, MSN, OCNS, BCCT Senior Researcher
Nancy Hepp, MS, BCCT Project Manager

Reviewer
Barry D. Elson, MD, BCCT Advisor

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