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FOR PATIENTS®

2021

Colon Cancer

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Contents

6	Colon cancer basics
14	Treatment planning
24	Overview of treatments
34	Nonmetastatic colon cancer
42	Metastatic colon cancer
52	Survivorship
58	Making treatment decisions
65	Words to know
68	NCCN Contributors
69	NCCN Cancer Centers
70	Index

1

Colon cancer basics

- 7 The colon
- 8 Colon polyps
- 9 About cancer
- 9 Colon cancer stages
- 13 Review



Colon cancer is one of the most commonly diagnosed cancers in the United States. Improvements in its detection and treatment have led to better outcomes for patients. This chapter provides some basic information about colon cancer that will help prepare you for treatment.

The colon

The colon is the longest part of the large intestine, also known as the large bowel. The large intestine is a long tube-shaped organ

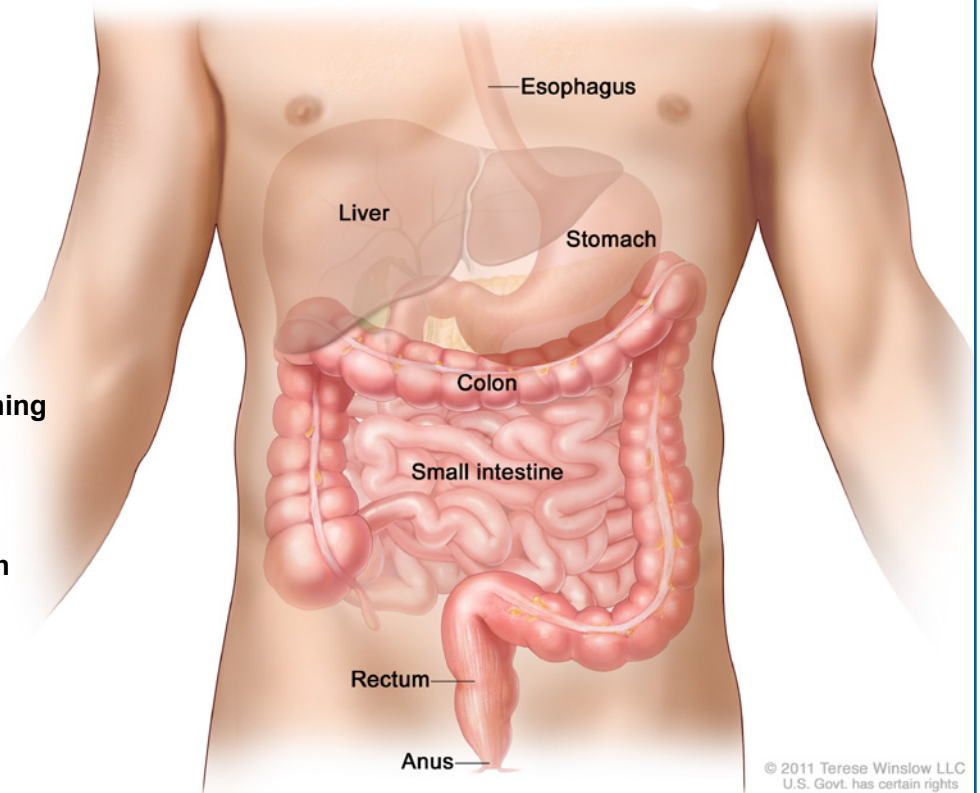
that forms the last part of the digestive system. The digestive system breaks down food for the body to use.

After being swallowed, food passes through the esophagus and into the stomach, where it is turned into a liquid. From the stomach, food enters the small intestine. In the small intestine food is broken down into very small parts to allow nutrients to be absorbed into the bloodstream.

Partly digested food then moves into the colon. The colon is the first and longest section of the large intestine. It is almost 5 feet long and has four parts: the ascending, transverse, descending, and sigmoid colon.

The colon

The colon is the first and longest part of the large intestine. The colon absorbs water from unused food, turning it into stool. Stool is held in the last section of the large intestine, called the rectum, until it exits the body through the anus.



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The first part of the colon is called the cecum. This pouch is about the size of a small orange. Sticking out from the cecum is a skinny tube called the appendix. It is closed at one end, and is about the size of a finger.

In the colon, water is absorbed from unused food, changing it from a liquid to a solid. This solid, unused food is called feces or stool. Stool then moves into the last section of the large intestine, called the rectum. Stool is held in the rectum until it exits the body through an opening called the anus.

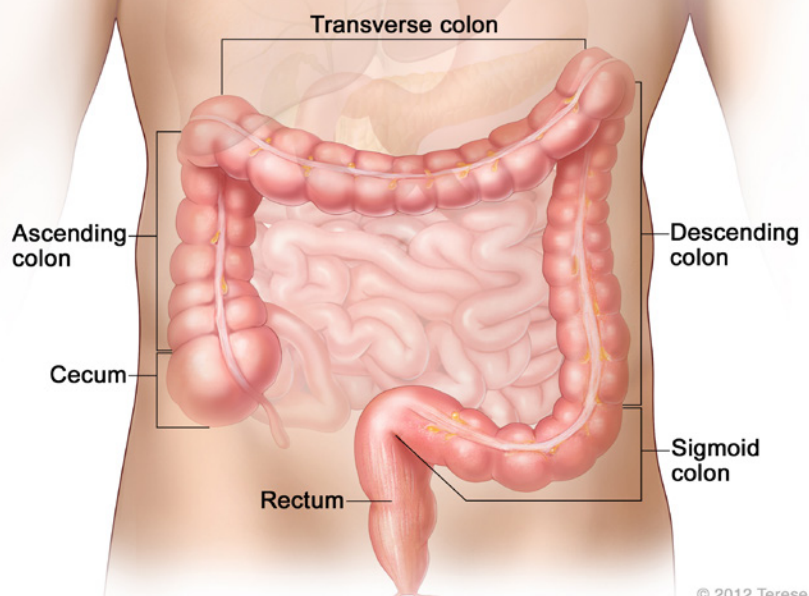
Colon polyps

A polyp is an overgrowth of cells on the inner lining of the colon wall. There are different types of polyps. Some types are more likely to turn into cancer than others. The most common type is called an adenoma. Adenomas are considered pre-cancerous because, while it may take many years, they can become invasive colon cancer. Cancer that forms in an adenoma is known as an adenocarcinoma. Adenocarcinoma is the most common type of colon cancer. Polyps that are highly unlikely to turn into cancer include hyperplastic and inflammatory polyps.

Parts of the colon

The colon is the longest part of the large intestine. It is almost 5 feet long and has four sections: the ascending, transverse, descending, and sigmoid colon.

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Removing polyps can prevent cancer before it occurs. Polyps can also be tested to make sure that cancer has not already started to develop. While most colon polyps do not become cancer, almost all colon cancers start in a polyp. Most polyps can be removed during a colonoscopy, using a minor surgical procedure called a polypectomy. More information on colon polyps is provided in *Part 4, Nonmetastatic cancer*.

About cancer

The human body is made of over 30 trillion cells. All cells have built-in instructions that tell them how to act. These instructions are called genes. Genes are a part of deoxyribonucleic acid (DNA). Changes called mutations in genes cause normal cells to become cancerous.

Cancer cells don't act like normal cells. Normal cells grow and then divide to make new cells when needed. They also die when old or damaged. Cancer cells make new cells that are not needed and do not die quickly when old or damaged. Over time, some types of cancer cells form a lump called a tumor.

Normal cells listen to signals from nearby cells telling them to "stop" when they get too close. Cancer cells ignore the "stop" signals from nearby cells and invade nearby tissues.

Normal cells stay in the area of the body where they belong. For example, stomach cells stay in the stomach. Cancer cells can break off and travel in lymph and blood to other parts of the body, where new tumors can form. This is called metastasis.

Colon cancer stages

The cancer stage is an assessment of the extent of cancer in the body. It is used to plan which tests may be needed and which treatments are best for you. Having a general idea of the structure of the colon wall is helpful for understanding how colon cancer is staged.

The colon wall is made of layers of tissue. Cancer starts in the innermost layer that comes in contact with food. This layer is called the mucosa. The next layer is the submucosa. It is made of connective tissue and contains mucus glands, blood and lymph vessels, and nerves. The submucosa is followed by a layer of muscle called the muscularis propria. The outer, fourth layer is called serosa (or adventitia).

If left untreated, cancer cells grow through the layers of the colon wall, towards the inside of the abdomen. The cancer can then invade structures or organs outside of the colon. Cancer cells can also break off from the colon tumor and travel through lymph or blood to nearby lymph nodes.

The American Joint Committee on Cancer (AJCC) tumor, node, metastasis (TNM) system is used to stage colon cancer. In the AJCC system, the following key pieces of information about the cancer are used to give it a stage:

- **T:** How far the tumor has grown into or through the colon wall
- **N:** Whether any lymph nodes have cancer in them
- **M:** Whether the cancer has spread to areas or organs outside the colon (metastasized)

The T, N, and M scores are combined to assign the cancer a stage. There are five stages of colon cancer. They are numbered 0, I (1), II (2), III (3), or IV (4). The stages are explained below.

Stage 0

There are abnormal cells on the innermost layer of the colon wall. These abnormal cells may become cancer and spread into deeper layers of the colon wall. Stage 0 colon cancer is also called carcinoma in situ of the colon.

Stage I

The cancer has grown into either the second or third layer of the colon wall. There is no cancer in nearby lymph nodes or in areas outside the colon.

Stage II

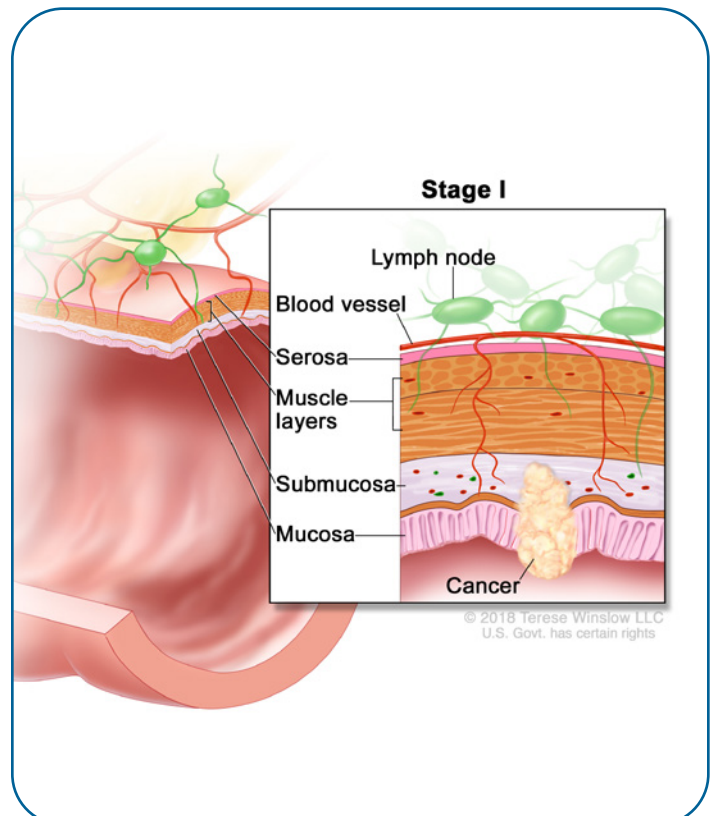
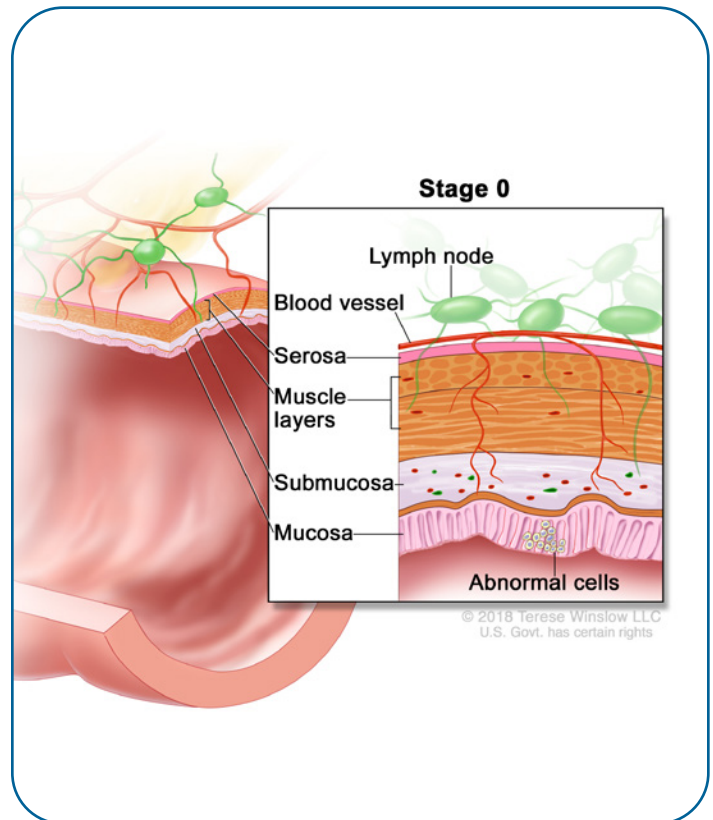
The cancer has grown into, or beyond, the fourth layer of the colon wall. There is no cancer in nearby lymph nodes or in areas outside the colon.

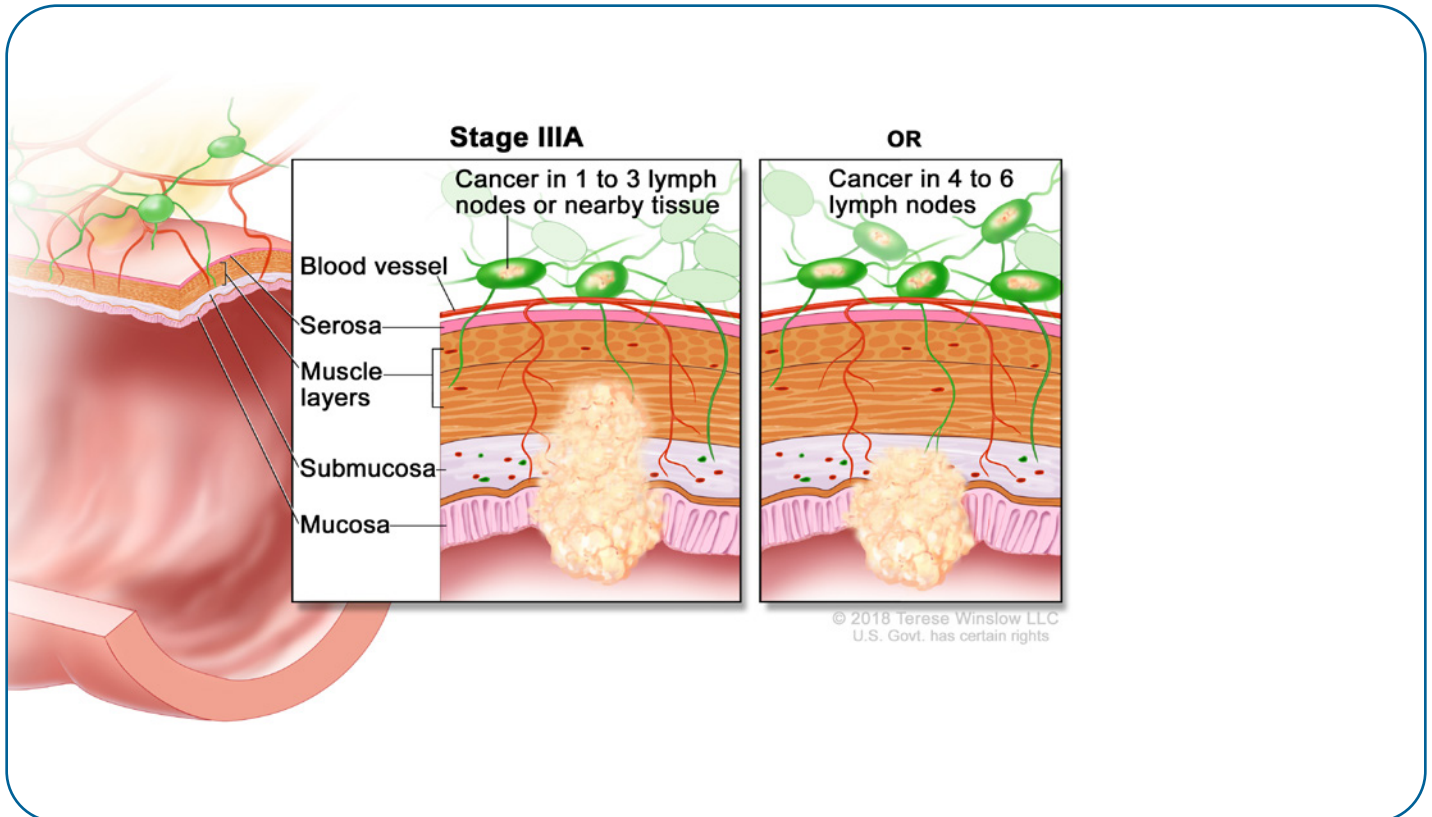
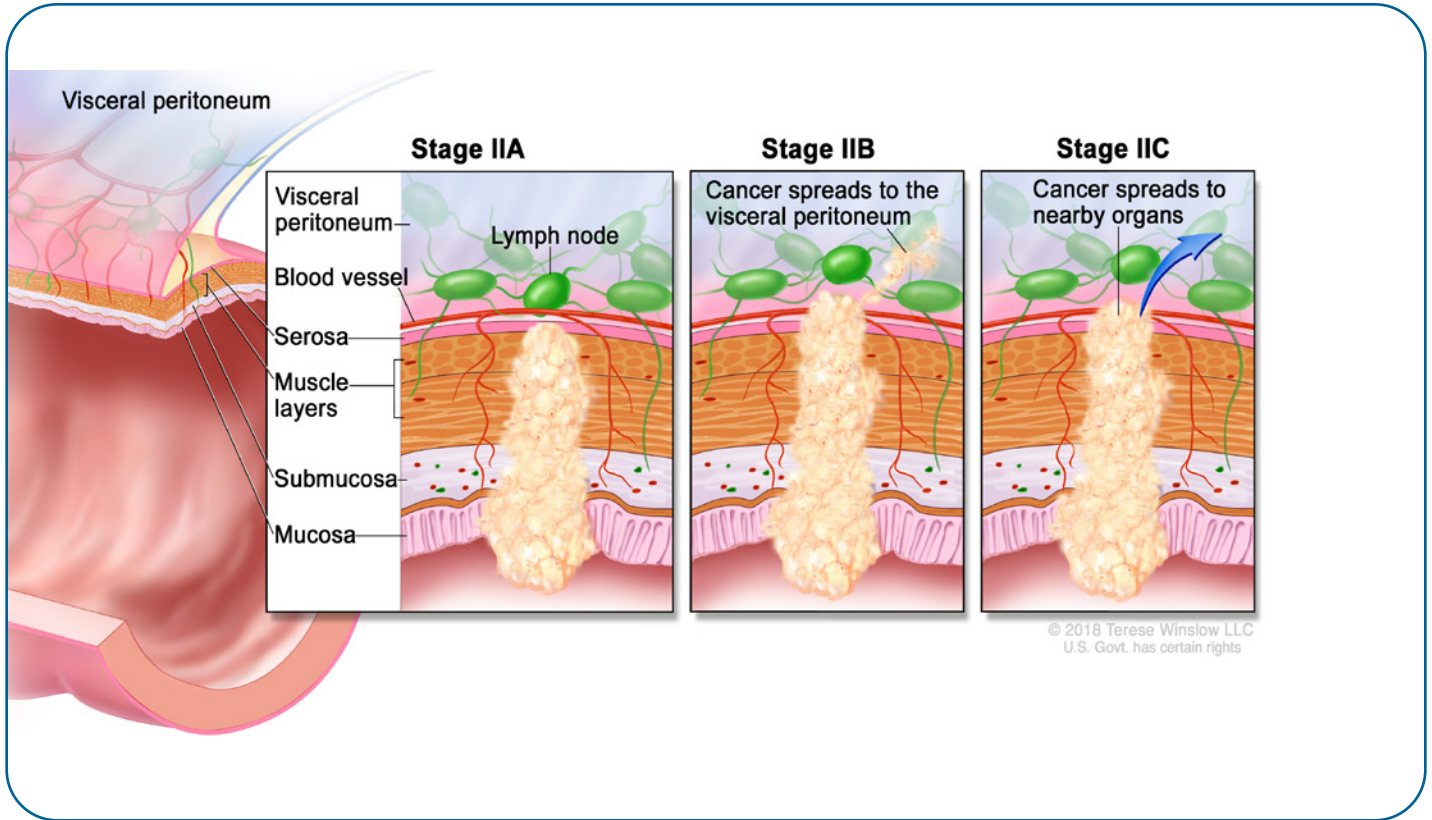
Stage III

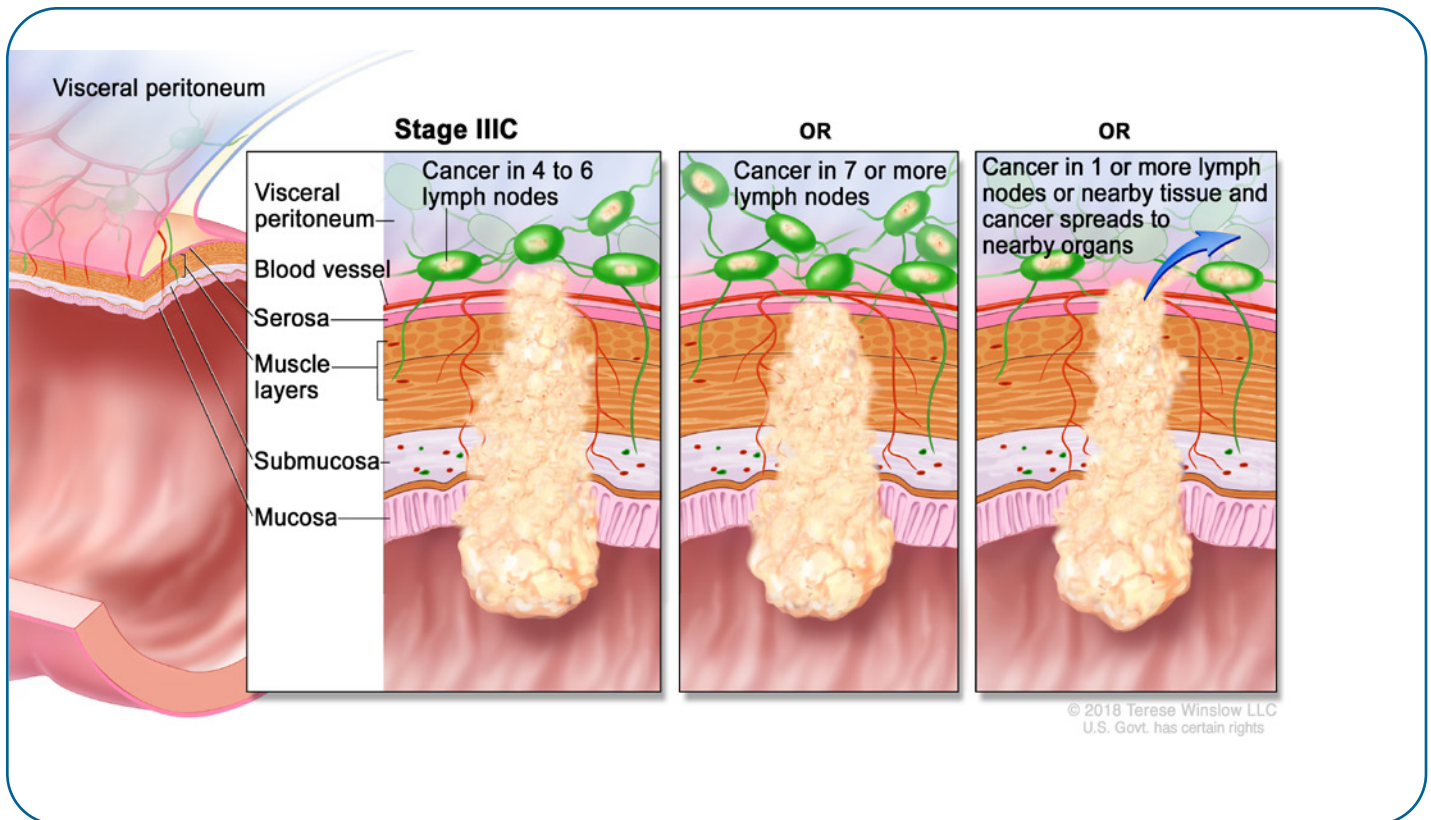
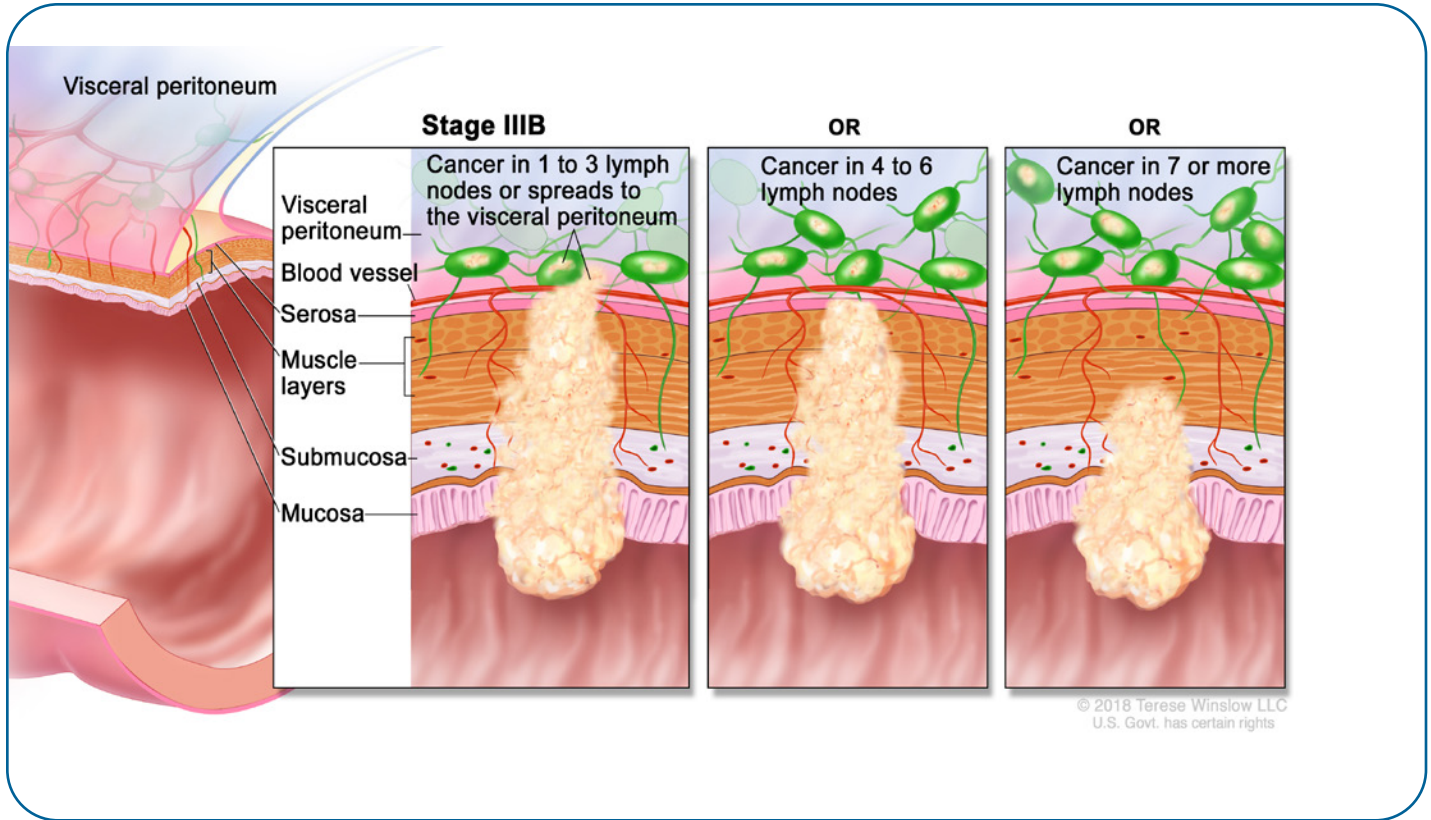
The cancer has spread from the colon to nearby lymph nodes or there are tumor deposits. Tumor deposits are small tumors in the fat around the colon.

Stage IV

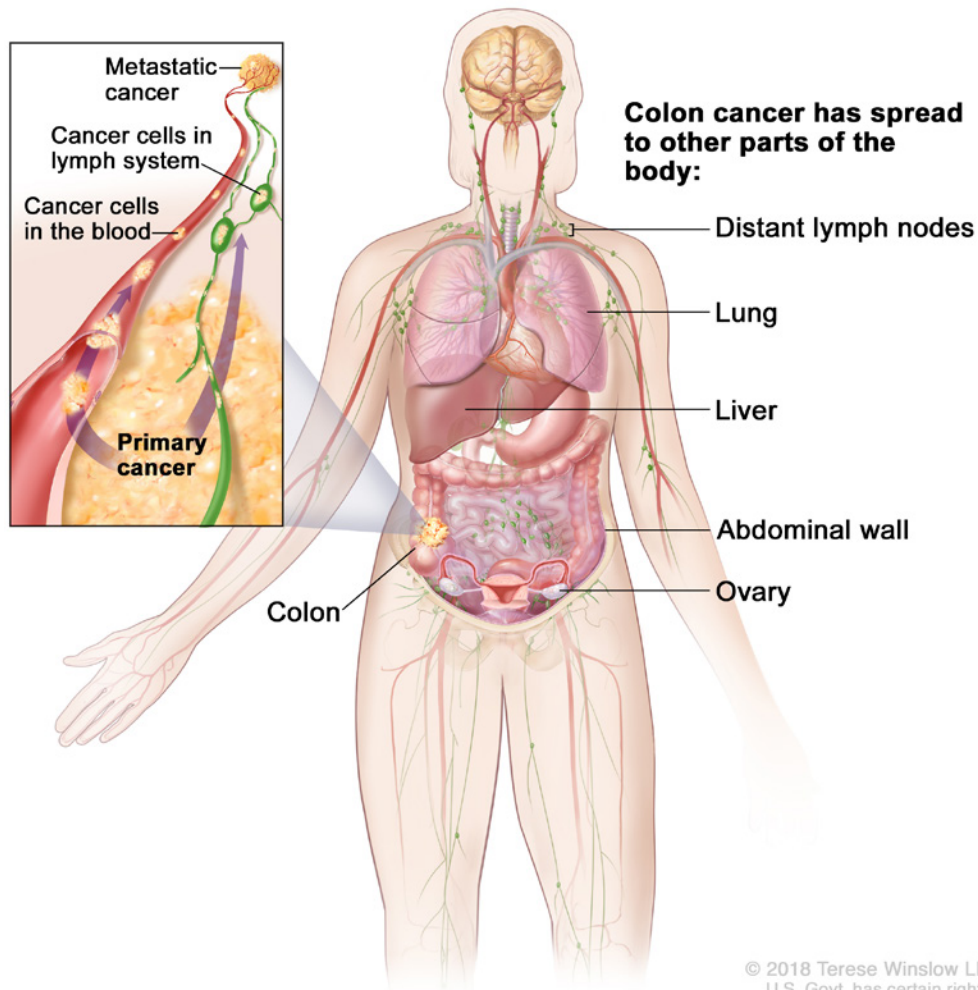
The cancer has spread to areas outside the colon and nearby lymph nodes. Colon cancer spreads most often to the liver and/or lungs.







Stage IV



Review

- The colon is the first and longest part of the large intestine.
- The colon has four parts: the ascending, transverse, descending, and sigmoid colon.
- Most colon cancers start in polyps called adenomas.
- If left untreated, cancer grows through the colon wall towards the inside of the abdomen.
- Cancer cells can spread to other body parts through lymph or blood. This is called metastasis.
- The stage is an assessment of the extent of cancer in the body.

2

Treatment planning

- 15 Health history
- 16 Biopsy
- 17 Colonoscopy
- 18 Blood tests
- 18 Imaging tests
- 21 Biomarker testing
- 22 Fertility and family planning
- 23 Review



Your doctors will make a treatment plan just for you. First, they need to gather information about your unique cancer and your general health. This chapter discusses testing and other steps needed to create your treatment plan.

Health history

Your medical history includes any health events and medicines you've taken in your life. It helps your doctors decide which treatments may be best for you. Colon cancer and other diseases can run in families. For this reason, your doctor will ask about the medical history of your blood relatives. It is important to know who in your family has had what diseases and at what ages. Your doctor may ask about the health of your siblings, your parents and their siblings, and your grandparents and their siblings.

Inherited cancer syndromes

Colon cancer most often occurs for unknown reasons. Some people, however, are more likely to get colon cancer than the average person. This is because a mutation in their DNA was passed down to them, causing a disorder that increases the risk of colon cancer. This is called an inherited cancer syndrome. There are two main inherited cancer syndromes for colon cancer—Lynch syndrome and familial adenomatous polyposis (FAP). Both are uncommon, occurring in fewer than 5 out of 100 people with colon cancer.

If your doctor thinks you might have an inherited syndrome, you will be referred to a genetic counselor. A genetic counselor can talk

with you and sometimes your family members about getting tested for syndromes related to colon cancer. To be tested, you must provide a sample of blood or saliva. A pathologist tests the sample for changes (mutations) in genes that cause these syndromes. It is very important to meet with a genetic counselor prior to having any genetic testing.

Lynch syndrome

People born with Lynch syndrome are at high risk of developing colon cancer and some other cancers. This syndrome is caused by inherited mutations of the genes that fix damaged DNA, called mismatch repair (MMR) genes. NCCN experts recommend testing everyone with colon cancer for problems with the MMR genes. This helps determine who should be tested for Lynch syndrome. Only about 5 out of every 100 people with colon cancer have Lynch syndrome. Sometimes Lynch syndrome is referred to as hereditary non-polyposis colon cancer (HNPCC), but they are not exactly the same. Specific family history criteria must be met in order for a diagnosis of HNPCC to be made.

Familial adenomatous polyposis (FAP)

FAP is a rare inherited syndrome that can cause hundreds to thousands of polyps to form in the colon and rectum. The polyps start as benign (non-cancerous) growths, but over time they can turn into colon cancer. Cancer is likely to develop by age 50 in people with classic FAP. A milder form called attenuated FAP causes fewer polyps and usually starts later in life. Only about 1 in 100 people with colon cancer have FAP.

Biopsy

A biopsy involves removing small pieces of tissue from the colon, which are sent to a pathologist for testing. A biopsy of a colon polyp or of suspected colon cancer is usually done during a colonoscopy.

If colon cancer is suspected to have spread to areas outside the colon, such as the liver or lungs, a needle may be used to do the biopsy. In this case, a CT scan or ultrasound may be used to help guide the needle into the tumor in order to remove the tissue sample. You might hear this referred to as a fine-needle aspiration (FNA).

Each time tissue is removed from the body and tested for cancer, the findings are detailed in a document called a pathology report. One key finding included in the report is the cancer grade, which is different than the cancer stage.

The cancer grade is a score of how fast the cancer is expected to grow and spread. It is based on how abnormal the cancer cells look when viewed under a microscope. Higher scores mean that the cancer is likely to grow and spread quickly. There are 5 possible grades:

- GX: Grade cannot be assessed (undetermined grade)
- G1: Well differentiated (low grade)
- G2: Moderately differentiated (intermediate grade)
- G3: Poorly differentiated (high grade)
- G4: Undifferentiated (high grade)

Review your pathology report(s) with your doctor. Ask questions if you don't understand. This information can be complex. It's also a good idea to get a copy of your pathology report(s) and take notes.

Colonoscopy

A colonoscopy is a procedure that allows your doctor to examine your colon for polyps and other diseases. A colonoscope is the device used for the test. Part of it looks like a thin tube. It has a light and camera. This part will be inserted into your anus and gently guided through your large intestine until it reaches the cecum.

You may be put on a liquid diet for 1 to 3 days before the test. You may also take a laxative or an enema the night before. This will clean out your intestine. Right before the test, you may be given a sedative to lessen any pain. You will likely wear a hospital gown. The test will be performed while you lie on your side.

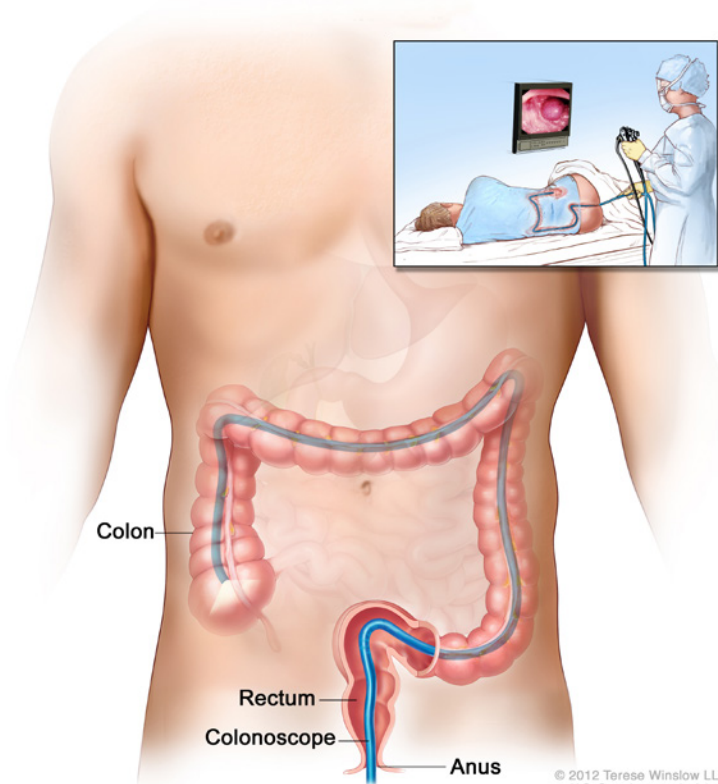
To see better, gas may be pumped into your intestine to make it bigger. You may be asked to shift a little to help your doctor guide the device. A picture of your colon will be viewed by your doctor on a screen. If a polyp is found, a cutting tool will be inserted through the tube to remove it.

A colonoscopy takes about 30 to 60 minutes. Afterward, you may stay for another hour for any drugs that were used to wear off. However, you'll still need someone to drive you home. The next day, you will likely feel normal. Contact your doctor if you have severe pain, vomiting, bloody stool, or weakness.

Colonoscopy

A colonoscopy is a procedure that allows your doctor to look for and remove any abnormal tissue from the colon. A thin device is inserted through the anus, up the rectum, and into the colon. The device has a light, a camera, and a cutting tool.

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Blood tests

Blood tests are used to look for signs of disease. A needle will be inserted into your vein to remove a sample of blood. The needle may bruise your skin and you may feel dizzy from the blood draw. Your blood sample will then be sent to a lab where a pathologist will test it. A pathologist is a doctor who is an expert in testing cells to find disease.

Complete blood count

A complete blood count (CBC) measures the number of blood cells in a blood sample. It includes numbers of white blood cells, red blood cells, and platelets. Cancer and other health problems can cause low or high counts.

Chemistry profile

A chemistry profile, also known as a comprehensive metabolic panel (CMP), measures the level of certain substances in the blood, such as metabolites, electrolytes, fats, and proteins. The levels of these substances provide important information about how well your kidneys, liver, and other organs are working.

CEA blood test

When colon cancer spreads, it can cause high or low levels of chemicals in the blood. One example is a high carcinoembryonic antigen (CEA) level. CEA is normally low in healthy adults. Pregnant women and smokers may have higher CEA levels. High CEA levels could mean that the cancer has spread beyond the colon.

Imaging tests

Imaging tests make pictures (images) of the insides of your body. They can show areas of cancer in the body. This information helps your doctors stage the cancer and plan treatment.

A radiologist is a doctor who is an expert in interpreting these images. Your radiologist will convey the imaging results to your cancer doctor (oncologist). This information helps your doctor plan the next steps of care.

Your treatment team will tell you how to prepare for these tests. You may need to stop taking some medicines and stop eating and drinking for a few hours before the scan. Tell your team if you get nervous when in small spaces. This is known as claustrophobia. You may be given a type of medicine called a sedative to help you relax.

Some imaging tests use contrast. Contrast is a substance that is injected into the bloodstream. It makes the pictures clearer. Some people have an allergic reaction to contrast. Tell your doctor if you've had problems with contrast in the past.

Computed tomography (CT)

CT takes many pictures of the inside of the body using x-rays. A computer combines the x-rays to make one detailed picture. The picture is saved for later viewing by a radiologist. CT is the primary imaging test used to determine the extent of colon cancer in the body. It can show areas of cancer in nearby and distant sites.

In a few select situations, CT may be combined with positron emission tomography (PET). PET/CT is not often used for colon

cancer. It may be used to help determine if surgery is an option for metastatic disease, or in the rare event that you cannot have contrast for CT or MRI. PET involves first injecting a radioactive drug (a “sugar tracer”) into the body. The radiotracer is detected with a special camera during the scan. Cancer cells appear brighter than normal cells because they use sugar more quickly.

MRI

Magnetic resonance imaging (MRI) uses a magnetic field and radio waves to make pictures. It is not often used to plan treatment for colon cancer. Your doctor may order an MRI if the CT scan was unclear. MRI is most often used to get a better look at the liver or rectum if needed. Contrast should be used.

Getting an MRI is much like getting a CT scan. In some cases, the area of the body being imaged is placed within a narrowed coil device. The coil device looks like a brace. It covers your body from below your chest to the top of your legs. It sends and receives radio waves. Straps may be used to help you stay in place. An MRI may cause your body to feel a bit warm. If MRI is being used to better see cancer near the rectum, an enema may be required or a gel may be inserted into the rectum beforehand.



What to expect: CT scan

- You will lie face-up on a table that moves through a tunnel-like machine.
- A substance called contrast will be used to make the pictures clearer.
- The contrast will be injected into your vein and mixed with a liquid you drink.
- The contrast may cause you to feel flushed or get hives.
- You will be alone during the scan, but a technician will be nearby. You will be able to hear and talk to the technician.
- You may hear buzzing or clicking during the scan.
- Tell your doctor if you get nervous in tight spaces.

CT scan

CT with contrast is the primary imaging test used to determine the extent of colon cancer in the body. CT takes many pictures of the inside of the body using x-rays. A computer combines the x-rays to make one detailed picture.



MRI

MRI makes pictures of areas inside the body without using radiation. Not everyone with colon cancer will need an MRI. Your doctor may order it to help determine if you have colon or rectal cancer, or if results of other imaging tests were unclear.



Biomarker testing

Treatment options for patients with advanced colon cancer may include targeted therapy or immunotherapy. Like chemotherapy, these are medicines that work throughout the body to treat cancer. Unlike chemotherapy, these newer therapies are most effective at treating cancers with specific features, called biomarkers. Biomarkers can include proteins made in response to the cancer and changes (mutations) in the DNA of the cancer cells.

Biomarker testing is used to learn whether your cancer has any targetable features. If it does, targeted therapy or immunotherapy may be a treatment option if needed. The results of biomarker testing can also be used to determine whether you meet the criteria for joining certain clinical trials. Testing for biomarker mutations involves analyzing a piece of tumor tissue in a laboratory.

Other names for biomarker testing include molecular testing, genomic testing, tumor gene testing, and mutation testing. Biomarkers used for colorectal cancer treatment planning are described below.

For everyone with colon cancer

MMR/MSI testing

In normal cells, a process called mismatch repair (MMR) fixes errors (mutations) that happen when DNA divides and makes a copy of itself. If a cell's MMR system isn't working right, errors build up and cause the DNA to become unstable. This is called microsatellite instability (MSI).

There are two kinds of laboratory tests for this biomarker. Depending on the method used, an

abnormal result is called either microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR). Both results mean the same thing. Tumors that **are not** MSI-H/dMMR are referred to as microsatellite stable (MSS) or mismatch repair proficient (pMMR).

MMR or MSI testing is recommended for everyone diagnosed with colon cancer. If the cancer is dMMR/MSI-H, you will also be tested for Lynch syndrome.

For metastatic colon cancer

If colon cancer has spread to other parts of the body, such as the liver or lungs, NCCN experts recommend testing for the tumor biomarkers described next.

KRAS and *NRAS* mutations

RAS is a family of genes that includes the *HRAS*, *KRAS*, and *NRAS* genes. Some colon cancers have mutations in the *KRAS* or *NRAS* genes. Genes work as instruction manuals for making important proteins. As a result, the proteins these genes make are overactive and can tell the cancer to grow.

BRAF mutation

Fewer than 10 out of 100 colon cancers have a mutation called *BRAF* V600E. This mutation may cause cancer cells to grow and spread quickly. If your cancer has this mutation, treatments that target abnormal *BRAF* may be helpful.

HER2 testing

HER2 is a protein involved in normal cell growth. Having too much HER2 can cause cancer cells to grow and spread quickly. Only about 3 to 5 out of 100 people with colon cancer have too much HER2. HER2 testing

is recommended for everyone with metastatic colon cancer unless there is a known *RAS* or *BRAF* mutation. It can help your doctor determine whether systemic therapies that target HER2 may help you.

Fertility and family planning

For unknown reasons, colon cancer is being diagnosed more often in young adults. Some cancer treatments can cause or contribute to infertility, which is the inability to have children. If you want the option of having children after treatment or are unsure, tell your doctors. There are ways for cancer patients to be able to have children after treatment. This is called fertility preservation.

If you are of childbearing age, your doctor will discuss any fertility-related risks of your treatment plan with you. You may be referred for counseling about fertility preservation options. Some fertility preservation options are described below.

Sperm banking

Sperm banking stores semen for later use by freezing it in liquid nitrogen. The medical term for this is semen cryopreservation.

Egg freezing

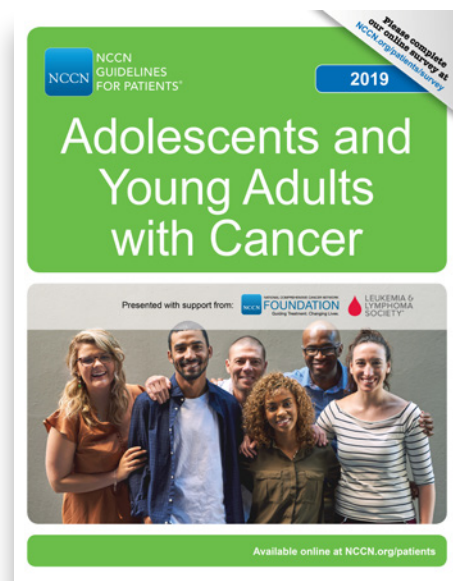
Like sperm banking, unfertilized eggs can be removed, frozen, and stored for later use. The medical term for this is oocyte cryopreservation.

Ovarian tissue banking

This method involves removing part or all of an ovary and freezing the part that contains the

eggs. The frozen tissue that contains the eggs can later be unfrozen and put back in the body.

For more information on this topic, see the *NCCN Guidelines for Patients: Adolescents and Young Adults with Cancer* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).



Review

- Everyone with colon cancer should be asked about their family health history.
- Inherited syndromes related to colon cancer include Lynch syndrome and FAP.
- CT with contrast is the primary imaging test used to determine the extent of colon cancer in the body.
- MMR or MSI testing is recommended for everyone diagnosed with colon cancer.
- Testing for mutated *KRAS/NRAS* and *BRAF* genes is recommended for everyone with metastatic colon cancer.
- HER2 testing is also recommended for everyone with metastatic colon cancer unless there is a known *KRAS/NRAS* or *BRAF* mutation.
- Young adults diagnosed with colon cancer should be counseled about fertility-related risks of treatment and options for fertility preservation.



Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

[NCCN.org/patients/response](https://www.nccn.org/patients/response)

3

Overview of treatments

25	Colon surgery
27	Systemic therapy
29	Local therapies for metastases
32	Clinical trials
33	Review



This chapter describes the treatments for colon cancer. If it is an option, surgery is the preferred and most effective treatment. Chemotherapy may be given after surgery, or in place of surgery if the cancer cannot be resected (removed by surgery).

Colon surgery

Another name for surgery that removes tissue, or all or part of an organ, is resection. Cancer that can be removed completely by resection is called resectable.

You may have more than one type of surgery. Surgery to remove liver or lung metastases is described in the “Local therapies for metastases” section on page 29. Your

treatment team will tell you how to prepare for and what to expect during surgery. You may need to stop taking some medicines to reduce the risk of severe bleeding. Eating less, changing to a liquid diet, or using enemas or laxatives will empty your colon for surgery. Right before surgery, you will be given general anesthesia.

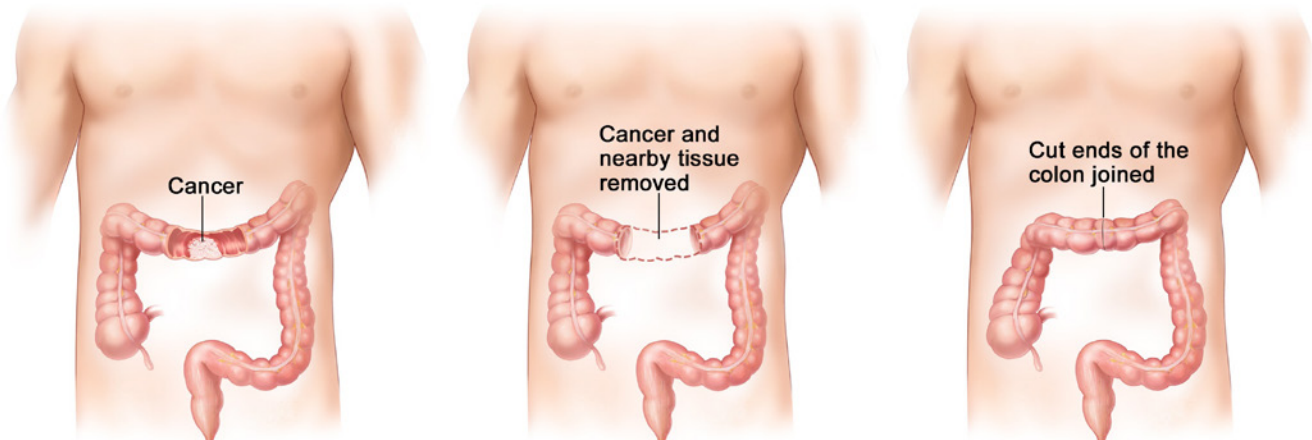
Colectomy

A colectomy is a surgery that removes the part of the colon with cancer. After the cancerous part is removed, the two healthy ends of the remaining colon are joined back together. They are either sewn or stapled together.

Lymph nodes near the tumor are also removed during colectomy. Lymph node removal is referred to as lymphadenectomy. At least 12 lymph nodes near the tumor should be

Colectomy

Surgery for colon cancer is called colectomy. It involves removing the cancerous part of the colon. The two healthy ends of the remaining colon are then attached to each other.



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removed and tested for cancer. Any abnormal-looking nodes will also be removed.

A colectomy can be done in two ways. The open method removes cancer tissue through a large cut in your abdomen. The minimally invasive method involves making a few small cuts. Tools are inserted through the cuts to see and remove part of your colon.

A colectomy can take 1 to 4 hours to complete. You may stay in the hospital for several days to recover. After surgery, you will be told what you can and cannot eat to prevent discomfort and help healing.

Colostomy

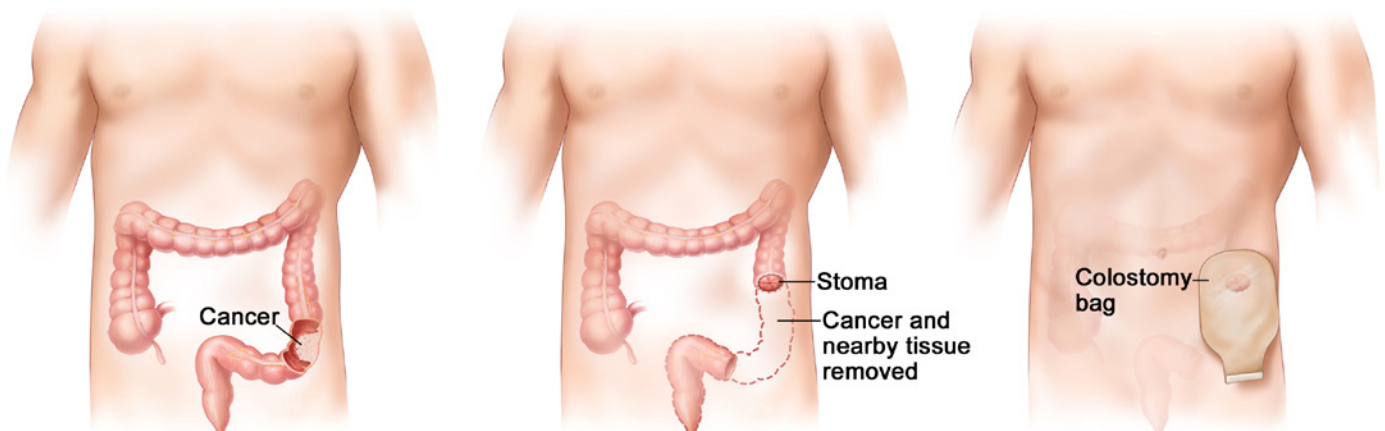
At the time of colectomy, some people may also have a procedure called a colostomy. This is done in cases where it may not be safe to reconnect the remaining sections of colon.

In a colostomy, the remaining upper part of the colon is attached to an opening on the surface of the abdomen. This opening is called a stoma. Stool exits the body through the stoma and goes into a bag attached to the skin. This is typically only needed for a short time (temporarily). For colon cancer surgery, it is rare for a colostomy not to be reversed with another operation. Colostomy is also known as diversion because it diverts (redirects) the flow of stool.

Colostomy

If the two healthy ends of the remaining colon cannot be safely reconnected after the cancer is removed, a colostomy may be performed. A colostomy connects a part of the colon to the outside of the abdomen. This creates an opening in your abdomen that allows stool to pass through. For colon cancer surgery, it is rare for a colostomy not to be reversed with another operation.

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Side effects of surgery

Surgery causes pain, swelling, and scars. Pain and swelling often fade away in the weeks following surgery. Scars from surgery do not disappear completely. As with any surgery, there is also a chance of complications. These include major blood loss, infection, heart attack, and blood clots. There can also be injury to nearby organs. Your surgical team will design care to try to prevent these risks.

There are short- and long-term side effects specific to colectomy. In the days or weeks following colon resection, food, digested debris, or stool may leak out where the colon was reconnected. This is known as anastomotic leak. It can cause pain, fever, and life-threatening infection.

Colectomy can also cause a change in bowel habits. You may experience changes in the frequency or urgency of your bowel movements.

It is common for scar tissue to form after abdominal surgery. In some cases, however, there is so much scar tissue that the bowel becomes obstructed (blocked). In rare cases, the bowel may become tightly wrapped around an area of scar tissue. This is an emergency that requires surgery.

A possible long-term effect of colon surgery is hernia. Hernia refers to organs pushing through tissues or muscles weakened by surgery.

Not all complications and side effects of surgery are listed here. Please ask your treatment team for a complete list of common and rare side effects.

Systemic therapy

Systemic therapy is the use of medicine to kill cancer cells. The medicine(s) travel in the bloodstream to reach cells throughout the body. Systemic therapy can kill healthy cells in addition to cancer cells. The damage to healthy cells can cause harsh side effects, such as hair loss, cracked skin, and mouth sores. Most commonly, systemic therapy is given intravenously. This means the medicine is slowly infused into the bloodstream through a vein.

Types of systemic therapy include chemotherapy, targeted therapy, and immunotherapy. If systemic therapy is planned, the regimen(s) given depends (in part) on:

- Whether the cancer has metastasized (spread to areas outside the colon)
- Whether surgery is possible or planned
- Whether the cancer has any biomarkers (see page 21 for more information)
- Your general health

Ask your treatment team for a full list of common and rare side effects of each systemic therapy you are receiving.

General information on the main types of systemic therapy is provided next. Specific recommendations for the use of systemic therapy is provided in *Part 4, Nonmetastatic colon cancer* on page 34 and *Part 5, Metastatic colon cancer* on page 42.

Chemotherapy

Chemotherapy is given in cycles of treatment days followed by days of rest. This allows your body to recover before the next cycle. Cycles vary in length depending on which drugs are used. Some commonly used combination chemotherapy regimens used to treat colon cancer are listed in [Guide 1](#).

The side effects of chemotherapy depend on many things (drug type, dosage, length of treatment) and are different for everyone. Common side effects include nausea, loss of appetite, diarrhea, hair loss, and mouth sores.

Regimens considered intensive that may be harsh on the body include FOLFOX, CAPEOX, FOLFIRI, and FOLFOXIRI. Any chemotherapy regimen that has “OX” in the name means the regimen includes oxaliplatin. Oxaliplatin can cause nerve damage to your fingers and toes. Symptoms include numbness, cramping, tingling, or pain in these areas.

Any chemotherapy regimen that has “IRI” in the name means it contains irinotecan. Irinotecan tends to cause abdominal cramping, nausea, diarrhea, and hair loss, but does not have the effects on nerves seen with oxaliplatin.

If regimens containing oxaliplatin and/or irinotecan are expected to be too harsh, your doctor may recommend 5-FU/leucovorin or capecitabine alone. However, these regimens can also cause potentially harsh side effects. Capecitabine can cause a side effect known as hand-foot syndrome. Symptoms include redness, swelling, and pain on the palms of the hands, bottoms of feet, or both. Sometimes blisters appear. Your dose of capecitabine may

be changed at the earliest signs of hand-foot syndrome.

Targeted therapy and immunotherapy

Unlike chemotherapy, targeted therapy and immunotherapy are most effective at treating cancers with specific features, called biomarkers. These newer types of systemic therapy may be treatment options for patients with advanced colon cancer.

Targeted therapies can target and attack specific receptors found on cancer cells. One type stops the growth of new blood vessels

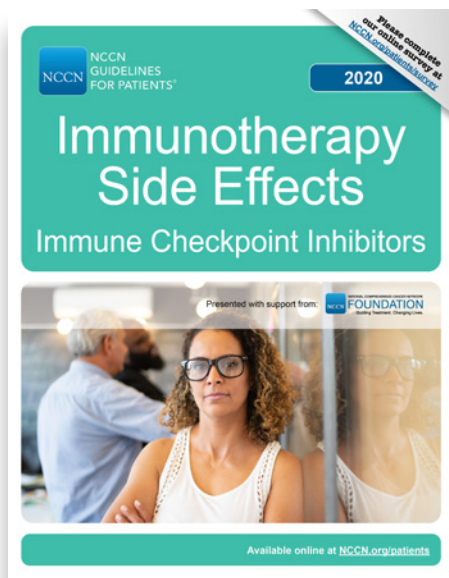
Guide 1 Combination chemotherapy regimens

FOLFOX	FOL = Leucovorin calcium F = Fluorouracil OX = Oxaliplatin
CAPEOX	CAPE = Capecitabine OX = Oxaliplatin
FOLFIRI	FOL = Leucovorin calcium F = Fluorouracil IRI = Irinotecan
FOLFOXIRI	FOL = Leucovorin calcium F = Fluorouracil OX = Oxaliplatin IRI = Irinotecan
5-FU/LV	FU = Fluorouracil LV = Leucovorin calcium

into colon tumors. Without the blood they need to grow, cancer cells “starve” and die. A second type stops the cancer cells from receiving signals to grow. Other types work in more than one way. A targeted therapy known as a biologic may be added to chemotherapy to treat advanced colon cancer.

The immune system is your body’s natural defense against infection and disease. Immunotherapy increases the activity of your immune system, improving your body’s ability to find and destroy cancer cells. Drugs called checkpoint inhibitors are a type of immunotherapy used to treat colon cancer.

For more information on the side effects of immune checkpoint inhibitors, see the *NCCN Guidelines for Patients Immunotherapy Side Effects: Immune Checkpoint Inhibitors* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines):



Local therapies for metastases

Resection

Surgery, also called resection, is the preferred way to remove colon cancer that has spread to the liver or lungs. Another name for surgery to remove a metastasis is metastasectomy. If resection is not possible, or is not expected to completely remove the metastases, treatment with other local therapies described in this section may be an option.

The methods of surgery for metastasectomy vary based on where the cancer has spread. Colon cancer spreads most often to the liver. Removing the cancerous part of the liver (liver resection) may be an option. If your doctor thinks your liver will be too small after the cancerous part is removed, you may need to have it enlarged. This is done using a procedure called portal vein embolization. This blocks the blood vessel to the liver tumor, which causes the healthy part of the liver to grow larger.

A port or pump may be placed during surgery to remove liver metastases. This allows chemotherapy medicines to be put directly into the liver after surgery. This is known as hepatic arterial infusion chemotherapy (HAIC). HAIC should only be received at treatment centers with experience in this method.

Radiation therapy

Radiation therapy uses high-energy rays to kill cancer cells. While radiation therapy is most often used to treat tumors in the liver and/or lungs, it may also be used in combination with chemotherapy to treat cancer in the colon that cannot be removed with surgery.

The type of radiation therapy used most often to treat metastatic colon cancer is external beam radiation therapy (EBRT). EBRT delivers radiation from outside the body using a large machine. The radiation passes through skin and other tissue to reach the tumor. Types of EBRT include three-dimensional conformal radiation therapy (3D-CRT), intensity-modulated radiation therapy (IMRT), and stereotactic body radiation therapy (SBRT). All types are conformal, which means that the radiation beams are shaped to the cancer site. This helps minimize damage to healthy tissue. The type used depends on the location and size of the tumor(s) and other factors.

If external radiation therapy is planned

A planning session, called simulation, is needed before treatment begins. After being guided into the treatment position, pictures of the cancer sites are made with an imaging test. Using the pictures, the radiation team plans the best radiation dose and number of treatments.

During treatment, you will lie on a table as you did for simulation. Devices may be used to keep you from moving. This helps to target the tumor. Radiation beams are aimed with help from ink marks on your skin or marker seeds in the tumor.

You will be alone in the treatment room. A technician will operate the machine from a nearby room and will be able to see, hear, and speak with you at all times. As treatment is given, you may hear noises. You will not see, hear, or feel the radiation. One session can take less than 10 minutes.



What are some side effects of radiation?

- Feeling tired and worn out
- Hair loss in the treated area
- Changes to urination and bowel movements
- Diarrhea
- Nausea/vomiting
- Late side effects can include infertility, lung scarring, heart disease, and second cancers
- Not all side effects are listed here. Ask your treatment team for a full list.

Intraoperative radiation

Radiation can also be aimed directly at the tumor site during surgery, after the tumor is removed. The goal is to destroy any cancer cells that may be left in the tissue that was connected to the tumor. This is known as intraoperative radiation therapy (IORT).

Ablation

Ablation destroys small tumors with little harm to nearby tissue. It is done by either an interventional radiologist or a surgeon.

Ablation may be used by itself if surgery isn't possible, or it may be used in addition to surgery. Currently, the most commonly used techniques are radiofrequency ablation (RFA) and microwave ablation. Using a probe placed directly into a tumor, these methods heat and kill cancer cells using high-energy radio and microwaves.

Hepatic arterial infusion chemotherapy (HAIC)

While chemotherapy is most often given intravenously to reach cells throughout the body, it can also be given directly to the liver to treat metastases. Using a port or pump that is placed during surgery, the drugs are funneled directly into the artery leading to the liver. NCCN experts advise that HAI should only be done at treatment centers with experience in this method.

Embolization

Embolization treats liver tumors with chemotherapy or radioactive beads. It is done by either an interventional radiologist or a surgeon. A catheter is inserted into an artery in your leg and guided to the tumor. Once in place, the beads are inserted into the blood vessel. The beads block blood flow to the tumor. Without blood, the cancer cells “starve” and die. The chemotherapy or radiation further damage the cancer cells and cause the tumor to shrink.

This treatment is a type of arterially directed catheter therapy. If radiation beads are used, it is known as selective internal radiation therapy. Embolization is an option for some people with liver metastases. It is given when chemotherapy is not an option.

External beam radiation therapy

A large machine aims radiation at the tumor, passing through skin and other tissue to reach it.



Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- ▶ Phase I trials study the safety and side effects of an investigational drug or treatment approach.
- ▶ Phase II trials study how well the drug or approach works against a specific type of cancer.
- ▶ Phase III trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- ▶ Phase IV trials study the long-term safety and benefit of an FDA-approved treatment.

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure

that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss with family, friends, or others you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your treatment team if you meet the requirements. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

What if I get the placebo?

A placebo is an inactive version of a real medicine. Placebos are almost never used alone in cancer clinical trials. All participants receive cancer treatment. You may receive a commonly used treatment, the investigational drug(s), or both.

Do I have to pay to be in a clinical trial?

Rarely. It depends on the study, your health insurance, and the state in which you live. Your treatment team and the research team can help determine if you are responsible for any costs.

**Finding a clinical trial****In the United States****NCCN Cancer Centers**

[NCCN.org/cancercenters](https://www.nccn.org/cancercenters)

The National Cancer Institute (NCI)

[cancer.gov/about-cancer/treatment/clinical-trials/search](https://www.cancer.gov/about-cancer/treatment/clinical-trials/search)

Worldwide**The U.S. National Library of Medicine (NLM)**

clinicaltrials.gov/

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)

1.800.4.CANCER (1.800.422.6237)

[cancer.gov/contact](https://www.cancer.gov/contact)

Review

- A colectomy is surgery that removes the part of the colon with cancer. Nearby lymph nodes are also removed and tested for cancer.
- Systemic therapy is the use of medicine to kill cancer cells throughout the body. Types of systemic therapy include chemotherapy, targeted therapy, and immunotherapy.
- Surgical resection is the preferred way to remove colon cancer that has spread to the liver or lungs.
- If surgical resection is not possible, or is not expected to completely remove the metastases, treatment with other local therapies may be an option.
- Other local therapies include radiation therapy, ablation, and embolization.
- Radiation therapy uses high-energy rays to kill cancer cells.
- Ablation kills cancer cells using high-energy radio and microwaves.
- Embolization blocks blood flow to a tumor and damages cancer cells with chemotherapy or radiation.
- Clinical trials give people access to investigational treatments that may, in time, be approved by the U.S. Food and Drug Administration (FDA).

4

Nonmetastatic colon cancer

-
- 35 Malignant polyps

 - 36 Colon cancer requiring surgery

 - 40 Surveillance

 - 41 Review



This chapter is a treatment guide for colon cancer that has not spread to areas far from the colon.

Malignant polyps

A polyp is an overgrowth of cells on the inner lining of the colon wall. The most common type is called an adenoma. Adenomas are considered pre-cancerous because, while it may take many years, they can become invasive colon cancer. Cancer that forms in an adenoma is known as an adenocarcinoma.

The two main shapes of polyps are sessile and pedunculated. Pedunculated polyps are shaped like mushrooms and stick out from the colon wall. They have a stalk and round top. Sessile polyps are flatter and do not have a stalk.

A polyp in which cancer has just started to grow is called a malignant polyp. Most polyps can be removed during a colonoscopy, using a minor surgical procedure called a polypectomy. In some cases, no further treatment is needed after a polypectomy.

Pedunculated polyp

Pedunculated polyps have a stalk and are mushroom-like in appearance.



Sessile polyp

Sessile polyps do not have a stalk and lie flatter against the lining of the colon wall.



In other cases, surgery (resection) of a bigger piece of the colon is needed. This depends on the size and shape of the polyp (pedunculated or sessile), the results of the polypectomy, and the results of testing the removed tissue. Before deciding whether resection is needed after a polypectomy, your doctor will review the results of testing with you and discuss your options.

Good polypectomy results

No further treatment is needed for a malignant **pedunculated** polyp that was completely removed in one piece and found to be low-risk based on testing. Malignant **sessile** polyps, however, are more likely to return after polypectomy and often have other poor treatment outcomes. For this reason, colectomy (surgery) is a recommended treatment option for sessile polyps—even those with good results of polypectomy and testing. See page 25 for information on colectomy. Observation is also an option for sessile polyps. If surgery is planned, see “Chemotherapy after surgery” on page 38 for next steps.

Other polypectomy results

If the polyp is not removed in one piece or testing of the removed polyp finds high-risk features, surgery may be needed. If high-risk features are found, more tests to determine the extent of the cancer are recommended. This includes blood tests and a computed tomography (CT) scan of the chest, abdomen, and pelvis. If testing finds that surgery is needed, surgery (colectomy) is recommended. Chemotherapy may be given after surgery. See “Chemotherapy after surgery” on page 38 for next steps.

Colon cancer requiring surgery

If the cancer is not found early enough to be removed by polypectomy, surgery (colectomy) is needed. See page 25 for information on colectomy.

Surgery is only an option if the colon tumor can be completely removed. If you are not a candidate for surgery, see “If surgery is not an option” on page 39.

The true extent of the cancer cannot be known until after surgery. It can be estimated, however, based on the results of testing.

Testing before surgery includes:

- Colonoscopy
- Biopsy
- Testing of removed tissue
- Mismatch repair (MMR) or microsatellite instability (MSI) testing
- Blood tests including complete blood count (CBC), chemistry profile, and carcinoembryonic antigen (CEA) level
- CT scan of the chest, abdomen, and pelvis with contrast
- Additional imaging tests as needed

More information on these tests can be found in *Part 2, Treatment planning* on page 14.

In some cases, chemotherapy is given before surgery. The goal is to shrink the colon tumor so it can be fully removed during surgery. Chemotherapy may be given before surgery if:

- The tumor has grown through the colon wall and invaded nearby structures
- There are numerous or very large lymph nodes suspected to be cancerous.

Chemotherapy regimens commonly used before surgery include FOLFOX and CAPEOX.

The tissue removed during surgery is sent to a pathologist. The pathologist assesses how far the cancer has grown within the colon wall and tests the removed lymph nodes for cancer. Based on the results of testing, the cancer stage is assigned. The stage helps determine whether chemotherapy is needed after surgery. See “Chemotherapy after surgery” on the next page.

If the bowel is blocked

In rare cases, a tumor may grow so large that it blocks the flow of stool. There are several possibilities when there is a blockage. One option is a colectomy that also unblocks the bowel. This is known as a one-stage colectomy.

Another option is colectomy with colostomy. In a colostomy, the remaining upper part of the colon is attached to an opening on the surface of the abdomen. This opening is called a stoma. Stool exits the body through the stoma and goes into a bag attached to the skin. This is typically only needed for a short time (temporarily). Colostomy is also known as diversion because it diverts (redirects) the

flow of stool. See page 26 for an illustration of colostomy.

Another possibility is that a colostomy may be done first, followed by a second surgery to remove the cancer. Lastly, a mesh metal tube called a stent may be placed first, followed by a second surgery to remove the cancer. The stent keeps the colon open, allowing gas and stool to pass.



We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better:

[NCCN.org/patients/feedback](https://www.nccn.org/patients/feedback)

Chemotherapy after surgery

Chemotherapy may be given after surgery. The goal is to kill cancer cells that may remain in the body. Whether chemotherapy after surgery is considered depends on:

- The cancer stage
- Whether the tumor is MSI-H/dMMR (for stage II colon cancer)
- The risk of the cancer returning after treatment (recurrence)

Stage I

Observation (no chemotherapy) is recommended after surgery for all stage I colon cancers.

Stage II

Observation (no chemotherapy) is recommended after surgery for most low-risk stage II cancers, especially MSI-H/dMMR tumors. Whether chemotherapy should be used after surgery is less clear for stage II cancers that **are not** MSI-H/dMMR. These are referred to as microsatellite stable (MSS) or mismatch repair proficient (pMMR). MSS/pMMR cancers can be observed or treated with chemotherapy. To help guide decision-making, your doctor will consider the risk of the cancer returning after treatment (recurrence). The risk for recurrence is based on findings during surgery and analysis of the removed tissue.

If chemotherapy is planned after surgery, recommended regimens for both high- and low-risk stage II colon cancer include capecitabine and 5-fluorouracil (5-FU)/leucovorin. FOLFOX and CAPEOX are recommended options for high-risk disease. [See Guide 2.](#)

Stage III

Chemotherapy is recommended after surgery for all stage III colon cancers. Recommended chemotherapy regimens include CAPEOX, FOLFOX, capecitabine, and 5-FU.

Chemotherapy after surgery is typically given for 3 to 6 months. The length of treatment depends on the chemotherapy regimen and the risk of recurrence. [See Guide 2.](#)

If surgery is not an option

Surgery may not be possible because of the location of the tumor or because of other health issues. In this case, treatment options include systemic therapy and chemoradiation. Chemoradiation involves treatment with both chemotherapy and radiation therapy.

If systemic therapy is planned, there are a number of possible regimens that may be used. The choice of regimen depends on whether the tumor has any biomarkers and

how well you are expected to tolerate certain systemic therapies. See page 21 for more information on biomarkers.

If chemoradiation is planned, chemotherapy medicines recommended for use with radiation include 5-FU and capecitabine. 5-FU is given by infusion; capecitabine is taken by mouth. If you are unable to tolerate either of these, a third option for use with radiation is bolus 5-FU/leucovorin. Bolus refers to the use of a single dose given over a short period of time.

Guide 2 Treatment after surgery

Stage I	Observation (no chemotherapy)	
Stage II	MSI-H/dMMR	Observation (no chemotherapy)
	MSS/pMMR	Observation OR chemotherapy with one of the following: <ul style="list-style-type: none"> • Capecitabine (6 months) (for low or high risk of recurrence) • 5-FU/leucovorin (6 months) (for low or high risk of recurrence) • FOLFOX (6 months) (only for high risk of recurrence) • CAPEOX (3 months) (only for high risk of recurrence)
Stage III	Chemotherapy with one of the following: <ul style="list-style-type: none"> • CAPEOX (3 months for low risk of recurrence; 3–6 months for high risk of recurrence) • FOLFOX (3–6 months for low risk of recurrence; 6 months for high risk of recurrence) • Capecitabine (6 months) • 5-FU (6 months) 	

After treatment with systemic therapy or chemoradiation, the size of the tumor will be checked to see if it is resectable (able to be removed with surgery). If the tumor does not become resectable, systemic therapy is continued. If the tumor becomes resectable, surgery is recommended.

After surgery, chemotherapy is recommended to kill any remaining cancer cells. Currently recommended regimens for use after surgery include FOLFOX, CAPEOX, capecitabine, and 5-FU/leucovorin. After chemotherapy, surveillance begins.

Surveillance

Follow-up testing is started when there are no signs of cancer after treatment. It is helpful for finding new cancer growth early.

Stage I

A colonoscopy is recommended 1 year after surgery for stage I colon cancer. If results are normal, the next colonoscopy should be in 3 years and then every 5 years. If an advanced adenoma is found, your next colonoscopy will be needed within 1 year. Advanced adenomas include polyps with a ruffled structure (villous), a polyp larger than 1 cm, or a polyp with pre-cancerous cells (high-grade dysplasia).

If you don't have any symptoms, other testing is not needed on a regular basis. Imaging tests may be ordered if your doctor thinks the cancer may have come back or spread.

Guide 3

Surveillance for stage II and stage III colon cancer

Medical history and physical exam	Every 3–6 months for first 2 years, then every 6 months for 3 more years
CEA blood test	Every 3–6 months for first 2 years, then every 6 months for 3 more years
CT of chest, abdomen, and pelvis	Every 6–12 months for 5 years
Colonoscopy	<p>No prior total colonoscopy: 3 to 6 months after surgery</p> <p>Prior total colonoscopy: 1 year after surgery</p> <p>If no advanced adenoma, repeat in 3 years, then every 5 years</p> <p>If advanced adenoma, repeat in 1 year</p>

Stages II and III

In addition to colonoscopy, surveillance for stages II and III colon cancer includes physical exams, CEA blood tests, and CT scans. Rising CEA levels may be a sign that colon cancer has returned. CT scans can find metastases, should any develop. The recommended schedule for surveillance testing is shown in [Guide 3](#).

In addition to surveillance testing, a range of other care is important for cancer survivors. See *Part 6, Survivorship* on page 52 for more information.

Review

- No further treatment is needed for a malignant pedunculated polyp that was completely removed in one piece and found to be low risk based on testing.
- Malignant sessile polyps are more likely to return after polypectomy than pedunculated polyps. In addition to observation, surgery is an option for sessile polyps.
- If the cancer is not found early enough to be removed by polypectomy, surgery (colectomy) is needed. If surgery is not possible, systemic therapy and chemoradiation are options.
- Chemotherapy may be given before surgery if the tumor has grown through the colon wall and invaded nearby structures or if there are many lymph nodes with cancer.
- Observation (no chemotherapy) is recommended after surgery for all stage I cancers and most low-risk stage II cancers, especially MSI-H/dMMR tumors.
- After surgery, stage II cancers that are not MSI-H/dMMR can be observed or treated with chemotherapy. The risk of recurrence based on the results of surgery and testing will be considered.
- Chemotherapy is recommended after surgery for all stage III colon cancers.
- Colonoscopies are used to monitor for the return of stage I colon cancer. Your doctor may also recommend physical exams and CEA blood tests.
- Surveillance for stages II and III includes physical exams, CEA blood tests, colonoscopies, and CT scans.

5

Metastatic colon cancer

43 Stage IV colon cancer

48 Metastasis at recurrence

51 Review



Colon cancer spreads most often to the liver, sometimes to the lungs, and less often to the abdomen or other areas. Cancer may have already spread by the time it is diagnosed. This is stage IV colon cancer. More commonly, metastases develop after treatment for non-metastatic colon cancer.

About half of people with colon cancer will develop metastases. Most will be liver metastases that cannot be removed with surgery. This section discusses both metastatic disease found at diagnosis (stage IV colon cancer) and metastatic disease that develops after treatment. Although both are considered metastatic cancer, there are some differences in how these types of cancer are treated.

Stage IV colon cancer

If cancer was found in areas far from the colon at the time you were first diagnosed with colon cancer, the cancer is stage IV. Testing for suspected (or known) stage IV colon cancer includes:

- Biopsy
- Colonoscopy
- Computed tomography (CT) scan of the chest, abdomen, and pelvis
- Blood tests including complete blood count (CBC), chemistry profile, and carcinoembryonic antigen (CEA) level
- Biomarker testing:
 - *RAS* and *BRAF* mutations
 - HER2 (not needed if there is a *RAS* or *BRAF* mutation)
 - Mismatch repair (MMR) or microsatellite instability (MSI) (if not already done)
- Additional imaging tests as needed to help determine if surgery is an option

More information on these tests can be found in *Part 2, Treatment planning* on page 14.

Cancer in the liver and/or lungs

When possible, surgery is the preferred way to treat colon cancer that has spread to the liver or lungs. To determine if surgery is an option for you, your case should be evaluated by a surgeon that specializes in liver or lung surgery. If liver and lung metastases cannot be removed with surgery, the primary treatment for stage IV colon cancer is systemic therapy.

Systemic therapy

The chemotherapy regimens FOLFIRI, FOLFOX, CAPEOX, and FOLFOXIRI are commonly used first-line systemic therapy for stage IV colon cancer. A targeted therapy known as a biologic may also be included in the regimen. Biologics include bevacizumab (Avastin), panitumumab (Vectibix), and cetuximab (Erbix). Panitumumab and cetuximab are only used for tumors in the left side of the colon that have normal *KRAS*/*NRAS* and *BRAF* genes.

For MSI-H or dMMR tumors, immunotherapy with pembrolizumab (Keytruda) or nivolumab (Opdivo) may be an option. Nivolumab may be given with another immunotherapy called ipilimumab (Yervoy). There is not as much research available on this option. Talk to your doctor about immunotherapy versus chemotherapy if your cancer is MSI-H/dMMR.

Systemic therapy may shrink the tumors to a size small enough to be removed with surgery. If your doctors think that surgery might be possible, the size of the tumors will be checked with imaging about every two to three months during systemic therapy.

If the tumors do not become resectable (able to be removed with surgery), systemic therapy is typically continued. If the cancer progresses (gets worse), the regimen you receive next will depend on the initial systemic therapy regimen used, whether the tumor has any biomarkers, and how well you are expected to tolerate certain systemic therapies. See page 21 for more information on biomarkers.

If the tumors become resectable, surgery is recommended. The colon tumor and the metastases may be removed during one

surgery or in two separate surgeries. If you were being treated with bevacizumab, it will be stopped 6 weeks before surgery. Bevacizumab increases the risk of stroke and bleeding, especially in adults aged 65 or older. Bevacizumab can be re-started 6 to 8 weeks after surgery. Otherwise, it can slow healing. After surgery, most people will have more systemic therapy. In some cases, observation or a shortened course of chemotherapy may be possible. Systemic therapy received before, between, or after surgeries should not exceed 6 months. Following any systemic therapy given after surgery, surveillance begins. See page 47.

Surgical treatment options

There are several options that include both systemic therapy and surgery to treat stage IV colon cancer. Surgery is only an option if all of the tumors can be completely removed.

Systemic therapy received before, between, or after surgeries should not exceed 6 months. The treatment options are described next and shown in [Guide 4](#).

Option 1

This option starts with surgery to remove the colon tumor (colectomy) and the liver or lung metastases. The surgeries may be done at the same time or in two procedures. While surgery is preferred by NCCN experts to remove the metastases, other local therapies may be appropriate for patients with a limited number of small metastases. Local therapies include ablation and radiation therapy.

The next phase of this treatment option is chemotherapy. The goal is to kill any cancer cells that may remain in the body. Currently recommended chemotherapy regimens include

FOLFOX, CAPEOX, capecitabine, and 5-FU/leucovorin. After chemotherapy, follow-up care and monitoring for the return of cancer begins.

Option 2

This option starts with chemotherapy. Currently recommended chemotherapy regimens for use before surgery include FOLFOX, CAPEOX, FOLFIRI, and FOLFOXIRI. Advantages of chemotherapy before surgery can include:

- You may receive early treatment of possible cancer not yet found
- Knowing your response to chemotherapy early can help with treatment planning
- If the cancer grows while receiving chemotherapy, you can avoid local treatment

Disadvantages of having chemotherapy before surgery therapy can include:

- The cancer does not respond to treatment and grows
- The cancer responds to treatment but shrinks so much that it is undetectable, and therefore unable to be surgically removed
- Surgery can no longer be performed because of liver injury caused by side effects

After 2 to 3 months of chemotherapy, the next step is surgery. The colon tumor and the metastases may be removed during one surgery or in two separate surgeries.

The next phase of this treatment option is more chemotherapy. Chemotherapy regimens currently recommended for use after surgery

Guide 4

Treatment options involving surgery for stage IV colon cancer

Option 1

Surgery and/or local therapy → Chemotherapy

Option 2

Chemotherapy → Surgery → Chemotherapy

Option 3

Colon surgery → Chemotherapy → Metastasectomy → Chemotherapy

Option 4

Immunotherapy → Surgery **Note:** This option is only for dMMR/MSI-H tumors

include FOLFOX, CAPEOX, capecitabine, and 5-FU/leucovorin. After chemotherapy, follow-up care and monitoring for the return of cancer begins.

Option 3

This option starts with surgery to remove the colon tumor (colectomy), followed by 2 to 3 months of chemotherapy. Currently recommended regimens include FOLFOX, CAPEOX, FOLFIRI, and FOLFOXIRI. Surgery to remove the metastases follows chemotherapy.

The next phase of this treatment option is more chemotherapy. Chemotherapy regimens currently recommended for use after surgery include FOLFOX, CAPEOX, capecitabine, and 5-FU/leucovorin. After chemotherapy, follow-up care and monitoring for the return of cancer begins.

Option 4

For MSI-H/dMMR tumors, your treatment options may include immunotherapy (instead of chemotherapy) before surgery. There is not as much research available on this option. If your cancer is MSI-H or dMMR, talk to your doctor about immunotherapy versus chemotherapy before surgery. Following immunotherapy, the colon tumor and metastases are removed, either at the same time or in separate surgeries. After chemotherapy, follow-up care and surveillance begins.

Cancer in the abdomen

About 17 out of 100 people with metastatic colon cancer will also form tumors in the peritoneum. The peritoneum is the thin layer of tissue that lines the abdomen and covers most of the abdominal organs. The goal of treatment for most abdominal/peritoneal metastases is to relieve or prevent symptoms. The main treatment is systemic therapy.

Tumors growing in or around the intestines can cause a bowel obstruction. A bowel obstruction is a blockage of the small or large intestine by something other than stool (feces). If the intestines are blocked, stool is prevented from moving and leaving the body.

If the cancer is not causing a bowel blockage, systemic therapy is recommended. The regimen you receive will depend on whether the tumor has any biomarkers and how well you are expected to tolerate certain systemic therapies.

If the cancer is (or is expected to) block the bowel, you will first need care to unblock the bowel before beginning systemic therapy. This can be done using one of several surgical techniques, or with a mesh metal tube called a stent.

Cytoreductive surgery and HIPEC

Colon cancer that spreads to the abdominal cavity can be difficult to treat. In some cases, cytoreductive surgery and/or hyperthermic intraperitoneal chemotherapy (HIPEC) may be treatment options.

Cytoreductive surgery involves surgically removing all visible tumors. If the tumor cannot be separated from the surface of an organ, the organ may also need to be removed. In

HIPEC, a heated chemotherapy solution is put directly into the abdominal cavity through small tubes called catheters. The chemotherapy solution kills any remaining microscopic cancer cells without killing healthy cells.

Research is needed on whether the benefits of cytoreductive surgery and HIPEC outweigh the potential harms. The use of HIPEC in particular is very controversial. NCCN experts recommend that these methods only be considered for patients with minimal metastases that can be completely removed with surgery. These procedures should only be carried out at cancer centers experienced in these methods.

Surveillance

Surveillance for stage IV colon cancer includes colonoscopies, physical exams, CEA blood tests, and CT scans. Rising CEA levels may be a sign that colon cancer has returned. CT scans can help find new metastases. The recommended schedule for surveillance testing is shown in [Guide 5](#).

In addition to surveillance testing, a range of other care is important for cancer survivors. See *Part 6: Survivorship* on page 52 for more information.

Guide 5 Surveillance for stage IV colon cancer

Medical history and physical exam	Every 3–6 months for first 2 years, then every 6 months for 3 more years
CEA blood test	Every 3–6 months for first 2 years, then every 6 months for 3 more years
CT of chest, abdomen, and pelvis	Every 3–6 months for first 2 years, then every 6–12 months for 3 more years
Colonoscopy	<p>No prior total colonoscopy: 3 to 6 months after surgery</p> <p>Prior total colonoscopy: 1 year after surgery</p> <p>If no advanced adenoma, repeat in 3 years, then every 5 years</p> <p>If advanced adenoma, repeat in 1 year</p>

Metastasis at recurrence

If colon cancer returns after initial treatment of localized colon cancer and is found in other areas of the body, such as the liver or lungs, it is called a distant recurrence. If surgery is possible, it is the best way to treat colon cancer that has spread to the liver or lungs. However, most liver and lung metastases cannot be removed using surgery. The primary treatment for distant recurrences of colon cancer that cannot be removed with surgery is systemic therapy.

Systemic therapy

If you've had chemotherapy with FOLFOX or CAPEOX within the past 12 months, the recommended options for systemic therapy are described next and shown in [Guide 6](#).

If you have not had recent treatment with FOLFOX or CAPEOX, your options for systemic therapy depend on prior chemotherapy received, whether the tumor has any biomarkers, and how well you are expected to tolerate certain systemic therapies. If one regimen stops working, there are other options that may work for you. These are called second- and third-line regimens.

Guide 6

Systemic therapy for distant recurrence - recent treatment with FOLFOX or CAPEOX

Regimen	May be given with
FOLFIRI or irinotecan	Bevacizumab Ziv-aflibercept Ramucirumab Cetuximab (normal <i>KRAS/NRAS</i> genes only) Panitumumab (normal <i>KRAS/NRAS</i> genes only)
Nivolumab (dMMR/MSI-H tumors only)	Ipilimumab
Pembrolizumab (dMMR/MSI-H tumors only)	—
Encorafenib + cetuximab or vemurafenib (BRAF V600E mutation positive)	—

FOLFOX or CAPEOX within last 12 months

Chemotherapy with FOLFIRI or irinotecan is an option. A targeted therapy known as a biologic may be given with either of these regimens. The biologics cetuximab and panitumumab are options for those with normal *KRAS/NRAS* and *BRAF* genes. Otherwise, bevacizumab, ziv-aflibercept (Zaltrap), or ramucirumab (Cyramza) may be given with FOLFIRI or irinotecan.

For MSI-H/dMMR cancers, immunotherapy with pembrolizumab (Keytruda) or nivolumab (Opdivo) may be an option. Nivolumab may be given with another immunotherapy called ipilimumab (Yervoy).

If the tumor has a *BRAF* V600E mutation, treatment with encorafenib (Braftovi) and either cetuximab (Erbix) or panitumumab (Vectibix) is an option.

Systemic therapy may shrink the tumors to a size small enough to be removed with surgery. If your doctors think that surgery might be possible, the size of the tumors will be checked about every two months during systemic therapy. If the cancer does not become resectable, systemic therapy is typically continued.

If the cancer becomes resectable, surgery is recommended. After surgery, most people will have more systemic therapy. Observation (no further treatment) may be an option in some cases. If systemic therapy is planned, the regimen may be different from what you had before surgery. Systemic therapy received before, between, or after surgeries should not exceed 6 months. When there are no signs of cancer, you can resume follow-up care and monitoring for the return of cancer.



If you are being treated with bevacizumab (Avastin), it should be stopped 6 weeks before surgery. It increases the risk of stroke and bleeding, especially in adults over 65. Bevacizumab can be restarted 6 to 8 weeks after surgery. Otherwise, it can slow healing.

Surgical treatment options

There are two options that include surgery to treat colon cancer that has returned and spread to the liver and/or lungs. Surgery is only an option if all the tumors can be totally removed. The treatment pathways also include chemotherapy, either before or after surgery.

Resection first

This option starts with surgery to remove the metastases. Local therapies such as ablation or radiation therapy may be appropriate instead of surgery if there are a limited number of small metastases.

If you have not had any previous systemic therapy, the next step is chemotherapy. Currently recommended regimens for use after surgery include FOLFOX, CAPEOX, capecitabine, and 5-FU/leucovorin. When there are no signs of cancer, you can resume follow-up care and monitoring for the return of cancer.

If you have received treatment with chemotherapy before, options include more chemotherapy and observation. If prior chemotherapy included oxaliplatin, observation is recommended.

When there are no signs of cancer, you can resume follow-up care and monitoring for the return of cancer.

Chemotherapy first

This option starts with chemotherapy to shrink the metastases. Currently recommended regimens include FOLFOX, CAPEOX, capecitabine, and 5-FU/leucovorin. After 2 to 3 months of chemotherapy, the next step is surgery to remove the metastases. Local therapies such as ablation or radiation therapy

may be appropriate instead of surgery if there are a limited number of small metastases.

More chemotherapy usually follows surgery. However, observation (no treatment) will be an option for some people. The chemotherapy regimens recommended for use before surgery are also recommended after surgery. When there are no signs of cancer, you can resume follow-up care and monitoring for the return of cancer.

Review

- Metastasis refers to the spread of cancer cells to distant areas.
- If metastases are present at the time of diagnosis, it is stage IV colon cancer.
- Most commonly, metastases develop after treatment for non-metastatic colon cancer. This is known as a distant recurrence.
- Surgery is the preferred treatment for colon cancer that has spread to the liver or lungs. However, most liver metastases cannot be removed using surgery.
- Metastatic colon cancer that cannot be removed with surgery is treated with systemic therapy.

Supportive care is available for everyone with cancer. It isn't meant to treat the cancer, but rather to help with symptoms and make you more comfortable.

6

Survivorship

53 Your primary care doctor

54 Help with side effects

55 Healthy habits

56 More information

57 Review



Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors. Managing the long-term side effects of cancer and its treatment, staying connected with your primary care doctor, and living a healthy lifestyle are important parts of survivorship.

Colon cancer survivors may experience both short- and long-term health effects of cancer and its treatment. The effects depend on the colon cancer treatment(s) received. Surgery, systemic therapy (chemotherapy, targeted therapy, and immunotherapy), and radiation therapy all have unique potential side effects.

Staying connected with your primary care doctor and adopting healthy habits may help prevent or offset these effects. It can also help lower the risk of getting other types of cancer.

Your primary care doctor

After finishing cancer treatment, your primary care doctor will play an important role in your care. Your oncologist (cancer doctor) and primary care physician (PCP) should work together to make sure you get the follow-up care you need. Your oncologist will develop a survivorship care plan that includes:

- A summary of your cancer treatment history
- A description of the late- and long-term side effects you could have

- Recommendations for monitoring for the return of cancer
- Information on when your care will be transferred to your PCP. The plan should also outline specific responsibilities for both your cancer doctor and your PCP
- Recommendations on your overall health and well-being

Help with side effects

Diarrhea or incontinence

Colon surgery can cause changes to your bowel habits. You may experience changes in the frequency or urgency of your bowel movements. Diarrhea refers to having frequent and watery bowel movements. Incontinence is the inability to control urination (urinary incontinence) or bowel movements (fecal incontinence). The following may help with these side effects:

- Anti-diarrhea medicines
- Changing your diet
- Strengthening your pelvic floor
- Wearing protective undergarments

Nerve damage

The chemotherapy drug oxaliplatin can cause nerve damage to your fingers and toes. Symptoms include numbness, cramping, tingling, or pain in these areas. Acupuncture and/or heat may help. If you have painful nerve damage, a drug called duloxetine (Cymbalta) may provide some relief.

Ostomy care

If you have an ostomy, you may want to join an ostomy support group. Another option is to see a health care provider that specializes in ostomy care, such as an ostomy nurse. People with ostomies can still live very active lifestyles. However, it's a good idea to consult with an ostomy professional before undertaking vigorous physical activity

Experts recommend eating a healthy diet, especially one that includes a lot of plant-based foods (veggies, fruits, and whole grains).



Healthy habits

Monitoring for the return of cancer is important after finishing treatment. But it is also important to keep up with other aspects of your health. Steps you can take to help prevent other health issues and to improve your quality of life are described next.

Cancer screening

Get screened for other types of cancer. Your primary care doctor should tell you what cancer screening tests you should have based on your gender, age, and risk level.

Other health care

Get other recommended health care for your age and gender, such as blood pressure screening, hepatitis C screening, and immunizations (such as the flu shot).

Diet and exercise

Leading a healthy lifestyle includes maintaining a healthy body weight. Try to exercise at a moderate intensity for at least 30 minutes most days of the week. Talk to your doctor before starting a new exercise regimen.

Eat a healthy diet with lots of plant-based foods. A low glycemic index (GI) diet may help prevent the return of colon cancer. Low GI foods cause a slower and smaller rise in blood sugar levels compared to other carbohydrate-containing foods. Talk to your doctor about a low GI diet.

Drink little to no alcohol. This means no more than 1 drink/day for women, and no more than 2 drinks/day for men.

Aspirin

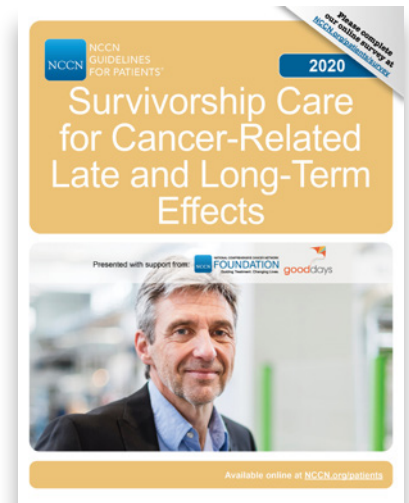
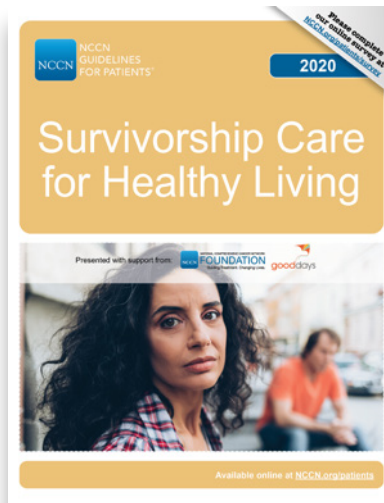
Talk to your doctor about taking aspirin every day to help prevent the return of colorectal cancers.

Quit smoking

If you are a smoker, quit! Your doctor will be able to provide (or refer you for) counseling on how to stop smoking.

More information

For more information on cancer survivorship see *NCCN Guidelines for Patients Survivorship Care for Health Living* and *Survivorship Care for Cancer-Related Late and Long-Term Effects* at [NCCN.org/patientguidelines](https://www.nccn.org/patientguidelines).



Cutting back on alcohol is an important part of staying healthy. Experts recommend no more than 1 drink per day for women, and no more than 2 drinks per day for men.



Review

- Survivorship focuses on the physical, emotional, and financial issues unique to cancer survivors.
- Your cancer doctor and primary care doctor should work together to make sure you get the follow-up care you need.
- The care recommended for you after cancer treatment should be detailed in a written survivorship care plan.
- It is important to live a healthy lifestyle after cancer. This means drinking little to no alcohol, eating a healthy diet, exercising, quitting smoking, and keeping up with other aspects of your health.

7

Making treatment decisions

59 It's your choice

59 Questions to ask your doctors

63 Websites



It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your doctor.

It's your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments like surgery or chemotherapy
- Your feelings about pain or side effects such as nausea and vomiting
- Cost of treatment, travel to treatment centers, and time away from work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor. If you take the time to build a relationship with

your doctor, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

Questions to ask your doctors

Possible questions to ask your doctors are listed on the following pages. Feel free to use these or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment. Use a notebook to record answers to your questions and keep track of all of your records.

Websites

American Cancer Society

cancer.org/cancer/colon-rectal-cancer.html

Cancer.Net

cancer.net/cancer-types/colorectal-cancer

CancerCare

[Cancer.org](https://cancer.org)

Cancer Support Community

cancersupportcommunity.org

ClinicalTrials.gov

clinicaltrials.gov

Colon Cancer Coalition

coloncancercoalition.org

Colon Club

Colonclub.com

Colorectal Cancer Alliance

ccalliance.org

Fight Colorectal Cancer

FightColorectalCancer.org

National Cancer Institute (NCI)

cancer.gov/types/colorectal

National Coalition for Cancer Survivorship

canceradvocacy.org/toolbox

National Comprehensive Cancer Network

NCCN.com



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And help make the
NCCN Guidelines for Patients
better for everyone!

NCCN.org/patients/comments



Words to know

abdomen

The belly area between the chest and pelvis.

ablation

Treatment using radiofrequency or cold to destroy cancer cells.

adenocarcinoma

Cancer in cells that line organs and make fluids or hormones. The most common type of colon cancer.

adenoma

The most common type of polyp and is the most likely to form cancer cells. Also called adenomatous polyps.

anus

The opening at the end of the digestive system that allows stool to pass out of the body.

biomarkers

Specific features of cancer cells. Biomarkers can include proteins made in response to the cancer and changes (mutations) in the DNA of the cancer cells.

biopsy

Removal of small amounts of tissue or fluid to be tested for disease.

cancer grade

How closely the cancer cells look like normal cells when viewed under a microscope.

cancer stage

Rating of the growth and spread of tumors.

carcinoembryonic antigen (CEA)

A protein that gets released by some tumors and can be detected in blood as a tumor marker.

carcinoma in situ

Abnormal cells on the innermost layer of the colon wall. These cells may become cancer and spread into deeper layers of the colon wall.

catheter

A flexible tube inserted in the body to give treatment or drain fluid from the body.

clinical trial

Research on a test or treatment to assess its safety or how well it works.

colectomy

Surgery to remove a part of the colon.

colon

The hollow organ in which eaten food turns from a liquid into a solid form.

colonoscope

A thin, long tube with a light and camera used to see the colon.

colonoscopy

Insertion of a thin tool into the colon to view or remove tissue.

colostomy

Surgery to connect a part of the colon to the outside of the abdomen and that allows stool to drain into a bag.

complete blood count (CBC)

A test of the number of blood cells.

computed tomography (CT)

A test that uses x-rays from many angles to make a picture of the inside of the body.

contrast

A substance put into your body to make clearer pictures during imaging tests.

embolization

Blockage of blood flow to a tumor with beads that emit either chemotherapy or radiation.

endoscopic polypectomy

Surgery to remove a polyp during a colonoscopy.

enema

Injection of liquid into the rectum to clear the bowel.

esophagus

The tube-shaped digestive organ between the mouth and stomach.

external beam radiation therapy (EBRT)

Treatment with radiation received from a machine outside the body.

familial adenomatous polyposis (FAP)

An inherited medical condition that increases the risk of colon cancer.

infusion

A method of giving drugs slowly through a needle into a vein.

intensity-modulated radiation therapy (IMRT)

Radiation therapy that uses small beams of different strengths based on the thickness of the tissue.

intraoperative radiation therapy (IORT)

Radiation therapy that is given inside the body at the end of an operation.

invasive cancer

Cancer cells have grown into the second layer of the colon wall.

lamina propria

Connective tissue within the mucosa of the colon wall.

large intestine

The digestive organ that prepares unused food for leaving the body.

laxative

Drugs used to clean out the intestines.

lymph

A clear fluid containing white blood cells.

lymph node

Small groups of special disease-fighting cells located throughout the body.

lymphadenectomy

Surgery to remove lymph nodes.

magnetic resonance imaging (MRI)

A test that uses a magnetic field and radio waves to make pictures of the insides of the body.

metastasectomy

Surgery to remove cancer that has spread far from the first tumor.

metastasis

The spread of cancer cells from the first (primary) tumor to a distant site.

microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR)

A biomarker (feature) of some colon cancers that is used to guide treatment. Everyone with colon cancer should be tested for this biomarker.

mucosa

The innermost layer of the colon wall.

muscularis propria

The third layer of the colon wall made mostly of muscle.

mutation

An abnormal change in the instructions (DNA) within cells for making and controlling cells.

needle biopsy

Removal of tissue or fluid samples from the body with a needle.

noninvasive cancer

Cancer cells have not grown into the second layer of the colon wall.

observation

A period of testing for cancer growth.

pathologist

A doctor who specializes in testing cells and tissue to find disease.

pedunculated polyp

A polyp shaped like a mushroom with a stalk.

pelvis

The area between the hip bones.

polyp

An overgrowth of cells on the inner lining of the rectum wall.

portal vein embolization

The blood vessel to the liver tumor is blocked causing the healthy part of the liver to grow larger.

positron emission tomography (PET)

Use of radioactive material to see the shape and function of body parts, and at times, highlight certain tumors within the body.

primary tumor

The first mass of cancer cells in the body.

progression

The growth or spread of cancer after being tested or treated.

radiation therapy

The use of high-energy rays to destroy cancer cells.

radiologist

A doctor that specializes in interpreting imaging tests.

rectum

The last part of the large intestine where stool is held until it leaves the body.

recurrence

The return of cancer after a cancer-free period.

serosa

The outer layer of the colon wall.

sessile polyp

A polyp that is flat.

small intestine

The digestive organ that absorbs nutrients from eaten food.

stereotactic body radiation therapy (SBRT)

Radiation therapy that uses precise, high-dose beams.

stool

Unused food passed out of the body; also called feces.

submucosa

The second layer of the colon wall made mostly of connective tissue.

supportive care

Treatment for the symptoms or health conditions caused by cancer or cancer treatment.

surgical margin

The normal tissue around the edge of a tumor that is removed during surgery.

three-dimensional conformal radiation therapy (3D-CRT)

Radiation therapy that uses beams that match the shape of the tumor.

tumor biomarker testing

Testing tumor tissue to look for targetable features called biomarkers.

tumor deposit

The presence of tiny tumors where the lymph drains from the tumor.

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NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • penncancer.org/cancer

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer
Center and Cleveland Clinic Taussig
Cancer Institute
Cleveland, Ohio
800.641.2422 • UH Seidman Cancer Center
uhhospitals.org/services/cancer-services
866.223.8100 • CC Taussig Cancer Institute
my.clevelandclinic.org/departments/cancer
216.844.8797 • Case CCC
case.edu/cancer

City of Hope National Medical Center
Los Angeles, California
800.826.4673 • cityofhope.org

Dana-Farber/Brigham and
Women's Cancer Center |
Massachusetts General Hospital
Cancer Center
Boston, Massachusetts
617.732.5500
youhaveus.org
617.726.5130
massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Huntsman Cancer Institute
at the University of Utah
Salt Lake City, Utah
800.824.2073
huntsmancancer.org

Fred Hutchinson Cancer
Research Center/Seattle
Cancer Care Alliance
Seattle, Washington
206.606.7222 • seattlecca.org
206.667.5000 • fredhutch.org

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmeltcancercenter.org

Robert H. Lurie Comprehensive
Cancer Center of Northwestern
University
Chicago, Illinois
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904.953.0853 • Florida
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James Cancer Hospital and
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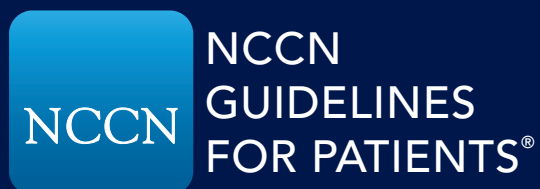
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Index

- ablation** 31, 33, 44, 50
- acupuncture** 54
- aspirin** 55
- BRAF*** 21, 23, 43–44, 48–49
- cancer staging** 9–13
- carcinoembryonic antigen (CEA)** 18, 36, 40–41, 43, 47
- carcinoma in situ** 10
- clinical trial** 21, 32–33, 60, 63
- colectomy** 25–27, 33, 36–37, 44–46
- colonoscopy** 9, 16–17, 35–36, 40, 43, 47
- familial adenomatous polyposis (FAP)** 15
- fertility** 22–23
- HER2** 21–23, 43
- hereditary non-polyposis colon cancer (HNPCC)** 15
- HIPEC** 46–47
- immunotherapy** 21, 28–29, 33, 44–46, 49, 53
- KRAS/NRAS*** 21–23, 43–44, 48–49
- lymphadenectomy** 25
- Lynch syndrome** 15, 21, 23
- metastasectomy** 27, 45
- microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR)** 21, 23, 36, 38, 41, 43–46, 48–49
- polypectomy** 9, 35–36, 41
- supportive care** 51
- surveillance** 40–41, 46–47
- survivorship** 53–57





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