**Risk Factors for Cancer**

* [Resize font](http://www.cancer.gov/about-cancer/causes-prevention/risk)
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It is usually not possible to know exactly why one person develops cancer and another doesn’t. But research has shown that certain risk factors may increase a person’s chances of developing cancer. (There are also factors that are linked to a lower risk of cancer. These are sometimes called protective risk factors, or just protective factors.)

Cancer risk factors include exposure to chemicals or other substances, as well as certain behaviors. They also include things people cannot control, like age and family history. A family history of certain cancers can be a sign of a possible inherited cancer syndrome. (See the [Hereditary Cancer Syndromes](http://www.cancer.gov/about-cancer/causes-prevention/genetics) section for more information about inherited genetic mutations that can cause cancer.)

Most cancer risk (and protective) factors are initially identified in epidemiology studies. In these studies, scientists look at large groups of people and compare those who develop cancer with those who don’t. These studies may show that the people who develop cancer are more or less likely to behave in certain ways or to be exposed to certain substances than those who do not develop cancer.

Such studies, on their own, cannot prove that a behavior or substance causes cancer. For example, the finding could be a result of chance, or the true risk factor could be something other than the suspected risk factor. But findings of this type sometimes get attention in the media, and this can lead to wrong ideas about how cancer starts and spreads.

When many studies all point to a similar association between a potential risk factor and an increased risk of cancer, and when a possible mechanism exists that could explain how the risk factor could actually cause cancer, scientists can be more confident about the relationship between the two.

The list below includes the most-studied known or suspected risk factors for cancer. Although some of these risk factors can be avoided, others—such as growing older—cannot. Limiting your exposure to avoidable risk factors may lower your risk of developing certain cancers.

* [Age](http://www.cancer.gov/about-cancer/causes-prevention/risk/age)
* [Alcohol](http://www.cancer.gov/about-cancer/causes-prevention/risk/alcohol)
* [Cancer-Causing Substances](http://www.cancer.gov/about-cancer/causes-prevention/risk/substances)
* [Chronic Inflammation](http://www.cancer.gov/about-cancer/causes-prevention/risk/chronic-inflammation)
* [Diet](http://www.cancer.gov/about-cancer/causes-prevention/risk/diet)
* [Hormones](http://www.cancer.gov/about-cancer/causes-prevention/risk/hormones)
* [Immunosuppression](http://www.cancer.gov/about-cancer/causes-prevention/risk/immunosuppression)
* [Infectious Agents](http://www.cancer.gov/about-cancer/causes-prevention/risk/infectious-agents)
* [Obesity](http://www.cancer.gov/about-cancer/causes-prevention/risk/obesity)
* [Radiation](http://www.cancer.gov/about-cancer/causes-prevention/risk/radiation)
* [Sunlight](http://www.cancer.gov/about-cancer/causes-prevention/risk/sunlight)
* [Tobacco](http://www.cancer.gov/about-cancer/causes-prevention/risk/tobacco)

**Cancer Management**

When cancer is suspected in an individual, either because of a screening test or because of signs and symptoms that lead the person to seek care, a host of services may be needed. Ideally the person would have access to diagnostic services and if a cancer is, in fact, diagnosed, services appropriate to the type and stage of cancer. For some people, this means potentially curative treatment with surgery, radiotherapy, or chemotherapy, or much more frequently, some combination of these modalities, applied by a multi-disciplinary medical team working together. Even at early treatable stages, and often as a result of treatment, palliative care for symptom control can be beneficial. For difficult-to-treat cancers, the many cancers of all types not seen until they are advanced beyond probable cure, and other cancers that advance despite treatment, palliative care alone may be most appropriate. Psychosocial services to help deal with the psychological and social impacts of cancer can be appropriate for virtually all people with cancer, and for the survivors of those who die from cancer. These approaches all fall into the “cancer management” category.

**Cancer Management: Diagnosis and Staging**

An accurate diagnosis is key to receiving appropriate care for cancer. Diagnostic tests include imaging, laboratory, and pathology techniques, in addition to physical examination. The same techniques are applicable to the initial diagnosis and staging and when reassessments are needed to determine a patient’s state at later time points. As is the case for other aspects of cancer management, new and more sophisticated (usually more expensive) diagnostic techniques have been added to those available traditionally, requiring choices to be made where resources are limited. A diagnosis may require one or more tests in sequence.

*Imaging* includes conventional X-rays, as well as ultrasonography, computed tomography ([CT](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d20/)) scanning, and magnetic resonance imaging ([MRI](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d71/)). These methods are used to visualize the anatomy of tumors. Two types of nuclear imaging techniques have been added more recently to cancer imaging modalities: Positron emission tomography ([PET](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d91/)) and single photon emission computed tomography ([SPECT](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d99/)). These techniques detect metabolic activity in cells, and can differentiate cancer cells by their different levels of activity.

*Laboratory tests* include tests on blood, urine, other fluids, and tissues. Specimens are collected by phlebotomy (blood drawing), fine-needle aspiration cytology or fine-needle-biopsy, and surgical procedures. In addition to tests looking directly for cancerous cells, other types of tests, e.g., to assess liver function or look for tumor markers (biological or chemical compounds that may increase when cancer is present) can provide information about the status of the cancer.

*Pathologic examination* for most solid tumors requires surgically excising a sample of the tumor, a biopsy. Cells found in body fluids are also evaluated by pathologic techniques. Microscopic evaluation of the tissue is carried out to determine the size of the tumor, its growth into other tissues and organs, the type of cancer cells, and the grade of the tumor (how closely the cancer cells resemble normal tissue).

Additional information about cancers is found during surgery. Surgical reports describe the size and appearance of tumors and may include observations about lymph nodes and nearby organs.

**Cancer Staging**

Once a cancer diagnosis is confirmed, further testing (using the same techniques) may be needed to determine the extent of the cancer. This information is captured in “staging systems,” which have developed over time. The principles are common to all cancers, but the details vary depending on the specific cancer. The common elements of staging are:

* location of primary tumor
* tumor size and number (if multiple)
* spread into lymph nodes
* cell type and grade of tumor (i.e., how closely the cancer cells resemble normal tissue)
* spread to distant sites (i.e., metastases)

The “[TNM](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d104/)” system is a widely used staging system (although not the only one). The [UICC](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d105/) is instrumental in updating and disseminating the TNM system. The initials T, N, and M stand for:

* T, tumor (extent of primary tumor)
* N, nodes (extent of spread to regional lymph nodes)
* M, metastases (presence or absence)

TNM Staging.

A typical example is a breast cancer classified as T3 N2 M0. This refers to a large tumor that has spread to nearby lymph nodes but has not metastasized to other parts of the body. [TNM](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d104/) classifications also correspond to numerical stages 0 through IV (expressed as Roman numerals)

Cancer Stages.

Another set of terms is also used to denote cancer stage ([National Cancer Institute, 2004](http://www.ncbi.nlm.nih.gov/books/NBK54025/)):

* In situ cancer is confined to the layer of cells in which it arose
* Localized cancer is limited to the organ in which it arose
* Regional cancer has spread beyond the primary site to nearly lymph nodes, or organs or tissues
* Distant cancer has spread from the primary site to distant parts of the body

Special classification systems are used for certain types of cancer, including cancers of the brain and spinal cord, leukemias and lymphomas, and other cancers in some circumstances (e.g., childhood cancers).

**Cancer Management: Surgery**

Surgery was the earliest form of cancer treatment and remains its mainstay where the range of cancer treatment is available. Until the middle of the 20th century, when chemotherapy and radiotherapy were developed as treatment modalities, surgical resection of tumors was the only available approach. For solid tumors today, long-term survival is usually dependent on surgical removal of the primary tumor (and a margin of normal tissue) and regional lymph nodes, often with additional treatment modalities. In the United States, about 90 percent of cures of solid tumors are through surgery alone or with other modalities. Cancers in which surgical resection is a major factor in cure include melanomas and cancers of the breast, colon, rectum, thyroid, stomach, and lung

The surgeries involved range from basic to highly complex, which bears on the types of settings in which they can be performed. The trend is toward less radical surgery than previously, using radiotherapy and/or chemotherapy to augment surgery. For example, bone or soft-tissue sarcomas of the extremities used to be treated by surgical amputation of the affected limb. Now, limbs are routinely spared by adding other treatment modalities to more conservative surgery.

Higher technology surgical techniques are common where resources are available. This includes the use of laparoscopic surgery and the extensive use of imaging, such as ultrasound, during surgery.

Not all surgery is done with curative intent (although intent might not be known until surgery is begun). When complete removal of a tumor is not possible, surgery is often still used to reduce (debulk) the tumor, which can prolong life and in some cases reduce symptoms (e.g., if the tumor is interfering with vital functions).

**Cancer Management: Radiotherapy**

Radiotherapy refers to the application of ionizing radiation (X-rays, γ-rays [gamma rays], or radioactive particles) for treatment. Radiation oncology is the medical discipline of treating malignant disease with radiation. Radiotherapy can be used curatively, as a single modality, or in conjunction with surgery, chemotherapy, or both. It can also relieve symptoms (palliate) in patients with incurable cancer. Radiotherapy has some limited medical uses in noncancerous conditions (e.g., keloid or “heaped-up” scars), but it is overwhelmingly a cancer treatment modality.

**How Radiotherapy Works**

Different types of cells—normal and malignant—vary in their susceptibility to ionizing radiation. Clinical radiotherapy schedules are designed to exploit the differences between normal tissues and tumors, so that as many malignant cells as possible are killed, while damage to normal tissue is minimized. In radical curative treatments, total radiation doses may be close to the tolerance of normal tissues. In palliative treatments, lower doses are the norm.

Some tumors, such as seminoma of the testis and lymphoma, are very sensitive to radiotherapy and can be cured with relatively low doses. Others, such as glioblastoma multiforme in the brain, are notoriously resistant, even to large doses.

A course of radiotherapy may be spread over days or weeks. This is known as *fractionating*, and the radiation delivered to a patient in a single treatment session is called a *fraction*. Fractionating allows normal tissues to repair much of the radiation damage, while tumor cells, which are less efficient at repair, do not recover. Each fraction of radiotherapy kills a certain proportion of the cancer cells in the irradiated region. A beam of radiation is called a *field*. A fraction consists of one or more fields delivered sequentially.

External-beam radiotherapy can be delivered by cobalt machines or linear accelerators (“linacs”), collectively known as “megavoltage machines.” Cobalt machines and linacs deliver very high-energy, highly focused beams that can reach deeper tumor tissues while depositing relatively small doses in the normal tissues through which they pass. Linacs produce the same intensity of radiation throughout operation, but the machines are more complex than cobalt machines and require greater manpower and attention to maintain them. These factors make cobalt machines—with replaceable cobalt sources—more appropriate in many [LMCs](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d64/). As the cobalt source decays, treatment time increases, decreasing the number of patients that can be treated per day. The half-life of cobalt is 5.3 years, so a source that is 5.3 years old will take twice as long to deliver the prescribed dose to a patient as a new source. An 11-year-old source will take *four* times as long as a new source to deliver the same dose.

**Side Effects of Radiotherapy**

Both early (acute) and late (chronic) side effects can occur after radio-therapy. The occurrence and severity depend on the body site being treated, the volume of normal tissue irradiated (the larger the volume, the higher the risk and severity of side effects), the total dose, and the rate of dose accumulation (the amount per week).

Early side effects result from damage to proliferating tissues (i.e., cells that continually divide and replace old cells with new ones) such as the lining of the gastrointestinal tract, or the skin. For example, radiotherapy to an abdominal tumor may damage the mucosa of the small bowel, causing malabsorption and diarrhea, but most patients recover completely within a few weeks when new cells have replaced the damaged ones.

Late reactions, which are much less common than acute side effects, occur months or years after treatment ends. They may result from damage to nonproliferating differentiated tissues, which cannot compensate for cell death by dividing to replace lost cells. These effects may be difficult to reverse and can be permanent or progressive. Examples include fibrosis of the skin, spinal cord damage, scarring of the lungs, and radiation-induced liver disease.

Side effects can be minimized by meticulous planning and delivery of radiotherapy. Late-reacting tissues are particularly sensitive to the size of each radiation dose, so they can be protected by giving a greater number of smaller fractions of radiation, provided the total dose is not too high.

Second cancers are an even rarer type of late effect. Especially in children, even relatively low doses of radiation increase the risk of developing another malignancy, unrelated to the one that was treated originally. Leukemias appear on average 7 years after exposure and solid tumors after 10 or 20 years.

**Curative Radiotherapy**

In high-income countries, at least half of all cancer patients treated with radiotherapy—alone or with surgery, chemotherapy, or both—are treated with the goal of achieving a cure. Radiotherapy is used by itself when it has the highest cure rate or because it is likely to have fewer side effects. Examples include treatment of advanced cervical cancer, pituitary tumors, deep-seated gliomas, nasopharyngeal cancer, and early-stage, low-grade lymphomas, including Hodgkin’s lymphoma.

Radiotherapy is preferred over surgery when surgery will result in the loss of an organ and the control of the tumor is similar. Examples include laryngeal cancer and prostate cancer. Surgery alone can be effective for small tumors. For large tumors, radiotherapy is often used with surgery to reduce tumor size or reduce the risk of tumor recurrence so that the whole tumor site can be treated with the least effect on the patient’s normal functioning. In general, radiotherapy is used along with surgery when:

* Organ preservation is desirable; an example is breast-conserving surgery (lumpectomy);
* The tumor is advanced with a high risk of local recurrence after surgery, such as rectal cancer;
* An inoperable cancer can be rendered operable, such as when advanced rectal cancers that are adhered to other organs, preventing complete excision, can be shrunk by radiation;
* The surgery included too small a margin of normal tissue around the tumor to preclude a high likelihood of local recurrence; radiotherapy reduces that likelihood.

Chemotherapy may improve the results of radiotherapy in the treatment of some cancer Radiotherapy can treat large primary tumors, and chemotherapy can work on disseminated micrometastases. The dose-limiting toxicities of radiotherapy and chemotherapy are different, which means that it is possible to deliver a higher overall dose of “treatment” with the two modalities than with one or the other. Other mechanisms are enhanced tumor response with two modalities, and the use of chemical agents to protect noral tissues from radiation damage, allowing a greater radiation dose.

Beneficial Interactions Between Radiotherapy and Chemotherapy.

**Palliative Radiotherapy**

Growing tumors cause symptoms by their physical presence, e.g., by pressing on adjacent organs or blocking passages or orifices. Radiotherapy can be used to shrink tumors directly causing symptoms. In many cases, it may reduce or eliminate the need for analgesics (including opioids).

Radiotherapy is effective for people with incurable lung cancer, alleviating shortness of breath, cough, and hemoptysis (coughing up blood). For breast cancer, radiotherapy can control fungating masses (large, rapidly growing tissue), and for prostate cancer it can be used to relieve urinary obstruction. Short-course radiotherapy (sometimes just a single treatment, or for more extensive disease, a few treatments) is effective in relieving pain from bone and brain metastases and compression of the spinal cord and various nerves

Radiotherapy can reverse the effects of spinal cord compression and prevent paraplegia.

With longer courses than those used for symptom relief, radiotherapy can prolong life for patients with some incurable cancers such as high-grade gliomas

**SUMMARY AND RECOMMENDATION**

The review of causes and risk factors and of cancer control elements sets the stage for the latter chapters of this report, where the greatest opportunities for cancer control are identified. What comes from this review is that a few causes and risk factors are prominent in cancers common in [LMCs](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d64/): tobacco use; infectious agents, particularly hepatitis viruses,[HPV](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d48/), and *H. pylori*; and dietary factors, too little exercise, and too much body mass. A lot of factors have smaller, yet not insignificant, effects. The factors vary with how easily they can be modified. Tobacco smoking is addictive and difficult for people to stop once started, yet certain interventions are effective

We have the tools now to prevent nearly all hepatitis B and most cancer-causing HPV infections. Changing behavior related to diet and exercise has proved exceptionally challenging in the high-income countries where work has been done, and there is little to offer in this regard to LMCs at the moment. In 10 years, new knowledge about behavior change and about the causes of cancer could allow greater scope for direct intervention to prevent cancers.

Cancer prevention includes an array of activities, some outside the health care system (e.g., increasing tobacco taxes), some in the primary care system (e.g., infant vaccination against [HBV](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d40/)), and others under more specialized conditions (e.g., screening for precancerous changes in the cervix). Which prevention activities any country can and will adopt will depend on their specific circumstances.

These decisions and others about cancer control at a national level are best approached through a formal process that weighs the opportunities against the costs within the country context. National cancer control planning and the development of national cancer control programs is the obvious means for making such decisions. In this area, we defer the details to [WHO](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d114/), [UICC](http://www.ncbi.nlm.nih.gov/books/n/nap11797/nap11797.app2/def-item/acronyms.gl1-d105/), and other organizations that provide guidelines and recommendations referenced in this chapter. No other specific recommendations come out of this chapter directly, but the discussion here leads to recommendations in the remainder of the report.