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Cancer Staging

Staging is the process of finding out how much cancer is in a person's body and where it's located. It's how the doctor determines the **stage** of a person's cancer.

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Why is cancer staging needed?

For most types of cancer, doctors need to know how much cancer there is and where it is (among other things) to help determine the best treatment options. For example, the best treatment for an early-stage cancer may be <u>surgery</u>¹ or <u>radiation</u>², while a more advanced-stage cancer may need treatments that reach all parts of the body, such as chemotherapy³, targeted drug therapy⁴, or immunotherapy⁵.

Of course, the stage of a cancer isn't the only factor used to decide which treatments might be best. Sometimes, cancers with different stages might be treated the same way, or cancers with the same stage might be treated in different ways. Many factors determine the best treatment options for each person.

A cancer's stage can also be used to help predict the course it will likely take, as well as how likely it is that treatment will be successful. Although each person's situation is different, cancers of the same type and stage tend to have similar outlooks.

The cancer stage is also a way for doctors to describe the extent of the cancer when they talk with each other about a person's cancer.

Not all cancers are staged. For example, <u>leukemias</u>⁶ are cancers of the blood cells and therefore typically have spread throughout the body by the time they are found. Most types of leukemias aren't staged the way cancers that form tumors are.

Exams and tests to stage cancer

Different types of exams and tests can be used to figure out a cancer's stage.

- Depending on where the cancer is located, a **physical exam** may give some idea as to how much cancer there is.
- Imaging tests⁷ like x-rays, CT scans, MRIs, ultrasound, and PET scans may also give information about how much and where cancer is in the body.
- <u>Endoscopy exams</u>⁸ are sometimes used to look for cancer. For these exams, an endoscope, which is a thin, lighted tube (usually with a small video camera on the end) is put inside the body to look for cancer.
- A biopsy often is needed to confirm a cancer diagnosis. Biopsies might also be needed to find out if a lump felt on an exam or if something seen on an imaging test in another part of the body is really from the spread of cancer. During a biopsy, the doctor removes a tumor or pieces of a tumor to be looked at in the lab. Some biopsies are done during surgery. But biopsies can also be done using a thin, hollow needle or through an endoscope. For more on biopsies, see <u>Testing Biopsy</u> and Cytology Specimens for Cancer⁹.
- Lab tests of cancer cells (from a biopsy or surgery) and blood tests can also be used to help stage some types of cancer.

Cancer can be staged at different times

Typically, a cancer is staged when it is first diagnosed, before any treatment is given. But in some cases, it is staged again after treatment has started.

Clinical staging

The **clinical stage** is an estimate of the extent of the cancer based on results of physical exams, imaging tests (x-rays, CT scans, etc.), endoscopy exams, and any biopsies that are done before treatment starts. For some cancers, the results of other

tests, such as blood tests, are also used in clinical staging.

The clinical stage is often a key part of deciding the best treatment options. It can also be used when trying to get an idea of what a person's outlook (prognosis) might be. For example, the survival rates for most types of cancer are based mainly on the stage at the time of diagnosis (see below).

Pathological staging

If surgery to remove the cancer is the first treatment, doctors can also determine the **pathological stage** (also called the **surgical stage**). The pathological stage relies on the results of the exams and tests done before the surgery, as well as what is learned about the cancer during surgery.

Sometimes, the pathological stage is different from the clinical stage (for instance, if the surgery shows the cancer has spread more than was seen on imaging tests). The pathological stage gives more precise information, which can be used to help determine what other treatments might be needed, as well as to help predict treatment response and outcomes (prognosis).

Post-neoadjuvant therapy (or post-therapy) staging

For some cancers, some treatment other than surgery (such as chemo, targeted drug therapy, or radiation) might be done first. The goal might be to try to shrink the tumor before surgery (in which case the treatment is called **neoadjuvant therapy**), or it might be done as the main treatment if it's not clear that surgery is going to be an option.

Staging might be done after this first treatment to help measure the cancer's response to treatment. This can be done the same way as clinical staging (if surgery hasn't been done yet), which can help determine what type of surgery should be done. Or it can be done after surgery (the same way as pathological staging), which might give more precise information.

Recurrence or retreatment staging

Staging might also be done again at some point if the cancer comes back (recurs) or progresses (grows or spreads without ever having gone away completely). This information can be used to help guide decisions about further treatment.

Does restaging a cancer change the original stage?

When a cancer is staged again after the initial staging, it is sometimes referred to as **restaging**. Often the same tests that were done when the cancer was first diagnosed (such as physical exams, imaging tests, endoscopy exams, biopsies, and maybe surgery) are done again.

With any type of restaging, the new stage classification is added to the original stage, but it doesn't replace it. The stage assigned at diagnosis is still the one that is most important when discussing statistics like survival rates (described below).

From a practical standpoint, however, the stage assigned to the cancer isn't always as important as making sure everyone understands how far the cancer has spread, and what this means going forward. For example, if a person is diagnosed with a stage II cancer that later is found to have spread to other parts of the body, they (and their health care provider) may now describe this as a 'stage IV' cancer, even though this isn't technically accurate. What's most important is that everyone understands that the cancer has spread, and that this information is used to guide future treatment decisions.

What goes into the stage: The TNM system

There are different types of systems used to stage cancer, but the most common and useful staging system for most types of cancer is the **TNM system**.

The American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) maintain the TNM classification system as a way for doctors to stage many different types of cancer based on certain common standards.

In the TNM system, the overall stage is determined after the cancer is assigned a letter or number to describe the tumor (T), node (N), and metastasis (M) categories.

- T describes the original (primary) tumor.
- **N** tells whether the cancer has spread to the nearby lymph **nodes**.
- M tells whether the cancer has spread (metastasized) to distant parts of the body

The primary tumor (T category)

When trying to determine how much and where the cancer is in the body, doctors first look at the **primary (main) tumor**, which is where the cancer started. The tumor's size, location, and whether it has grown into nearby areas can all be important. Doctors also check for other nearby tumors.

The **T category** can be assigned a letter or a number:

- **TX** means there's no information about the primary tumor, or it can't be measured.
- **T0** means there is no evidence of a primary tumor (it cannot be found).
- **Tis** means that the cancer cells are only growing in the layer of cells where they started, without growing into deeper layers. This may also be called **in situ** cancer **or pre-cancer**.
- A number after the T (such as T1, T2, T3, or T4) might describe the tumor size and/or amount of spread into nearby structures. The higher the T number, the larger the tumor and/or the more it has grown into nearby tissues.

The lymph nodes (N category)

<u>Lymph nodes</u>¹⁰ near the primary tumor usually are checked to find out if cancer has spread into them. Lymph nodes are small, bean-shaped collections of immune cells. Many types of cancer often spread to nearby lymph nodes before they reach other parts of the body.

The N category can be assigned a letter or a number:

- NX means there's no information about the nearby lymph nodes, or they can't be assessed.
- N0 means nearby lymph nodes do not contain cancer.
- A number after the N (such asN1, N2, or N3) might describe the size, location, and/or the number of nearby lymph nodes affected by cancer. The higher the N number, the greater the cancer spread to nearby lymph nodes.

Metastasis (M category)

Doctors might also look at other parts of the body to see if the cancer has spread. Cancer spread to parts of the body far from the primary tumor is known as **metastasis**.

The M category is assigned a number:

- M0 means that no distant cancer spread has been found.
- M1 means that the cancer has been found to have spread to distant organs or tissues.

Each cancer type has its own version of the TNM categories, so letters and numbers don't mean the same thing for every type of cancer. For example, for some types of cancer, the T categories describe the size of the main tumor, while for others they describe how deeply the tumor has grown into the organ it started in, or whether the tumor has grown into nearby structures (regardless of its size).

For some cancer types, TNM categories may also have subcategories. These are noted with lowercase letters after the category. For example, T3a or T3b.

Some cancer types may also have fewer category options than other cancer types. For instance, some cancers may not have an N3 category.

Other notations that can be part of TNM

Each of the T, N, and M categories might be written with a lowercase letter in front of it, showing if it's a clinical or pathological classification:

- A clinical stage is noted with "c" (for example, cT1)
- A pathological stage is noted with "p" (for example, pN2)

For staging that is done after treatment or after cancer recurrence/progression, a category might also be given another lowercase letter in front of it:

- For cancers that are restaged after neoadjuvant therapy (or other therapy), a "y" might be used in front of the category (for example, ycT1 or ypT2)
- For cancers that are restaged after recurrence or progression of the cancer, an "r" might be used in front of the category (for example, rcT1 or rpT2)

Other factors that can affect a cancer's stage

For some cancers, the values for T, N, and M aren't the only things that determine the stage. Some other factors that may be taken into account include:

Grade: For most cancers, the grade is a measure of how abnormal the cancer cells look under the microscope. This is also called **differentiation**. Grade can be important because cancers with more abnormal-looking cells tend to grow and spread faster.

The grade is usually assigned a number, with lower numbers (for example, G1) used for

lower grade cancers.

- In **low-grade (well-differentiated) cancers**, the cancer cells look fairly normal. In general, these cancers tend to grow slowly and often have a better outlook.
- In **high-grade (poorly differentiated) cancers**, the cancer cells look more abnormal. High-grade cancers often tend to grow quickly, so they may need different treatments than low-grade cancers.

Even when the grade doesn't affect a cancer's stage, it might still affect a person's outlook and/or treatment.

Cell type: Cancers in some parts of the body can start in different types of cells. Because the type of cancer cell can affect treatment and outlook, it can be a factor in staging. For example, <u>cancers of the esophagus</u>¹¹ are mainly either squamous cell cancers or adenocarcinomas. Squamous cell esophageal cancers are staged differently from esophageal adenocarcinomas.

Tumor location: For some cancers, the main tumor's location affects outlook and is taken into account in staging. The stage of cancer of the esophagus, for example, depends on whether the cancer starts in the upper, middle, or lower third of the esophagus.

Blood levels of tumor markers: For some cancers, the blood levels of certain substances (called tumor markers or biomarkers) can affect the stage of the cancer. For example, in <u>prostate cancer</u>¹², the level of prostate-specific antigen (PSA) in the blood is taken into account in assigning a stage.

Results of tests on the cancer cells: For some cancers, lab tests done on the cancer cells are an important part of staging. For example, in <u>breast cancer</u>¹³, the stage can be affected by whether or not the cancer cells have proteins called <u>hormone receptors</u>¹⁴ on them.

A person's age: For some types of cancer, such as <u>thyroid cancer</u>¹⁵, a person's age at the time of diagnosis can affect their outlook, so it is taken into account when assigning a stage.

Assigning an overall stage (stage grouping)

Once the values for T, N, and M (and any other factors that affect stage) have been determined, they are combined to assign an overall stage.

For most cancers, the stage is a Roman numeral from I (1) to IV (4). Stage I cancers are less advanced and often have a better prognosis (outlook). Higher stage cancers typically have spread farther (or have other concerning features), so they might require more intense (or different kinds of) treatment. Sometimes stages are subdivided as well, using capital letters (for example, stage III might be subdivided into stages IIIA and IIIB).

Some cancers also have a stage 0, which is often called carcinoma in situ. This means the cancer is still only in the layer of cells where it first started, and it has not spread any farther.

Other staging systems

Not all cancers are staged using the TNM system. For example:

- Staging systems other than the TNM system are often used for Hodgkin and non-Hodgkin lymphomas, as well as for some other cancers.
- The International Federation of Gynecologists and Obstetricians (FIGO) has a staging system for cancers of the female reproductive organs. The TNM stages closely match the FIGO stages, which makes it fairly easy to convert stages between these 2 systems.
- Most cancers in or around the brain do not have a formal staging system, since these cancers typically don't spread to lymph nodes or other parts of the body.
- Some types of leukemias aren't staged at all, because they're assumed to have already spread throughout the body by the time they're found. Instead, they're described using terms such as untreated, in remission, or recurrent/relapsed.

Along with the TNM (and other) staging systems, cancers can also be staged in a simpler way, using the US National Cancer Institute's **Surveillance**, **Epidemiology**, **and End Results (SEER) Summary Staging system**. To learn more, see 'Cancer staging for statistics purposes,' below.

How the cancer stage might affect a person's prognosis

Along with the type of cancer a person has, the stage of the cancer is one of the most important factors when doctors try to determine a person's prognosis (outlook).

Stages and survival rates

For many types of cancer, prognosis is often expressed as a survival rate. This is the

percentage of people with a certain type and stage of cancer who are still alive a certain amount of time (usually 5 years) after being diagnosed. For example, if the 5-year survival rate for a certain type and stage of cancer is 80%, it means that 80 out of 100 people who have that type and stage of cancer will still be expected to be alive after 5 years.

Survival rates can't tell for sure what will happen with any particular person, because many other factors can also affect prognosis (see below). But they can give doctors and patients a general idea of how likely it is that treatment will be successful.

Survival rates are nearly always based on the stage of the cancer at the time of diagnosis. These numbers don't apply if the cancer is restaged later on. For example, the 5-year survival rate of a cancer that is initially diagnosed as stage II and later spreads to another part of the body is not necessarily the same as that for a cancer that is initially diagnosed as a stage IV cancer (because it had already spread to another part of the body when first diagnosed).

This is important to understand because the information on our pages that discusses survival statistics refers to the stage when the cancer was first diagnosed.

Other factors can also affect prognosis

It's also important to understand that while the stage of the cancer is important, many other factors can also affect a person's outlook. Depending on the cancer type, other important prognostic factors might include:

- A person's age and overall health
- Whether the cancer cells have changes in certain genes, chromosomes, or proteins
- How the cancer responds to treatment

If you have questions about survival rates and how they might be affected by the stage of your cancer or other factors, be sure to talk to your cancer care team.

Cancer staging can be complex

Doctors are always learning more about cancer, how it grows and spreads, and how best to treat it. Over time, some of these findings are added to the staging systems for different types of cancer, which helps make them more accurate and valuable to both doctors and patients.

At the same time, adding these newer findings often makes the staging systems more complex than they were in the past, which can make it harder for people to understand them.

If you're not sure about the stage of your cancer or what it might mean for you, ask your doctor to explain it to you in a way you understand.

Cancer staging for statistics purposes

The AJCC TNM (and similar) staging systems are used most often to determine the stage of a person's cancer, which in turn might be used to help determine the best treatment options for them.

But for statistics purposes, such as for survival rates, cancer registries and researchers often use a simpler staging system for most cancers. This is the National Cancer Institute (NCI) Surveillance, Epidemiology and End Results (SEER) Summary Staging system.

The SEER Summary Stages are a basic way of recording how far a cancer has grown and spread from where it started. Because it uses simpler stage definitions, an advantage of this system is that it doesn't change over time (unlike the TNM stages, which are updated every 5 to 10 years). This allows statistics that are based on stages (such as survival rates) to be followed over time to look for trends.

SEER Summary Stages

The basic SEER Summary Stages for most cancer types are:

- In situ: The cancer cells are only in the layer of cells where they first started and have not grown into (invaded) nearby tissues in the organ. (Not all cancer types have an in situ stage.)
- Localized: The cancer is invading nearby tissue but is still only in the organ it started in.
- Regional: The cancer has grown outside of the organ where it started. It has grown
 into nearby organs or structures and/or it has spread to nearby lymph nodes. But
 the cancer hasn't spread to distant parts of the body.
- **Distant:** The cancer has spread to distant parts of the body, to other organs or structures **and/or** to distant lymph nodes.
- **Unknown:** There is not enough information to figure out the stage.

For more on staging and survival rates, see 'How the cancer stage might affect a person's prognosis', above.

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