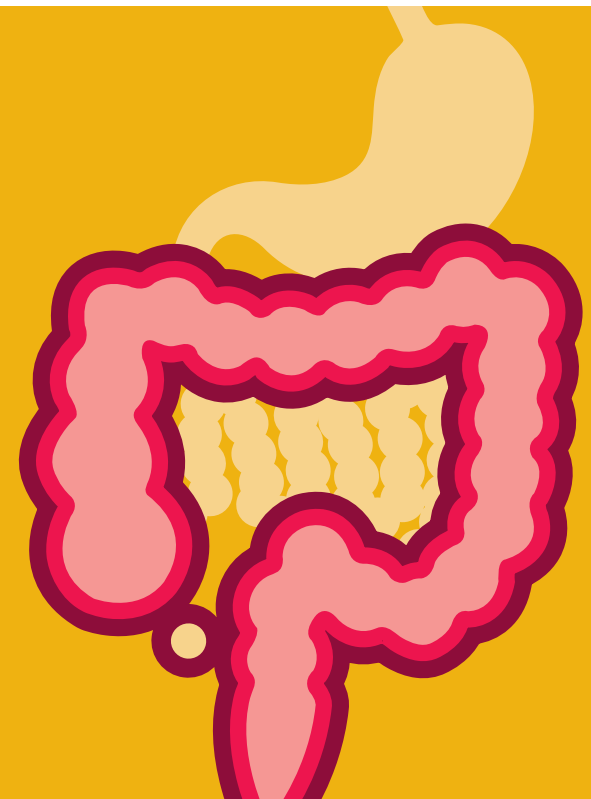


Colorectal cancer

A guide for journalists on colorectal cancer and its treatment



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Overview

Colorectal cancer is one of the most common cancers in the world, with over 1.2 million new cases diagnosed each year. Despite improvements in screening for early diagnosis, colorectal cancer remains one of the biggest cancer killers in the world and is responsible for over 600,000 deaths each year.^{1,2}

The standard treatments for colorectal cancer are surgery, chemotherapy and biological therapies. Early-stage (localised) cancer that has not spread (metastasised) from the original site has the potential to be cured if all the tumour cells can be successfully removed by surgery.

However, the early signs and symptoms of colorectal cancer are often ambiguous and can be confused with other diseases, such as Irritable Bowel Syndrome, Crohn's disease or peptic ulcers.³ This means that

many patients are diagnosed at a later-stage, when the cancer has already spread (metastasised) to other parts of the body. At this point, the cancer is more difficult to treat and the prognosis for the patient is significantly worse.⁴ Awareness and screening are therefore vital to improve the prognosis for patients.⁵

This guide provides an overview of colorectal cancer, including its incidence, risk factors, symptoms, diagnosis and treatment options.

Section 1

Colorectal cancer

i. What is colorectal cancer?

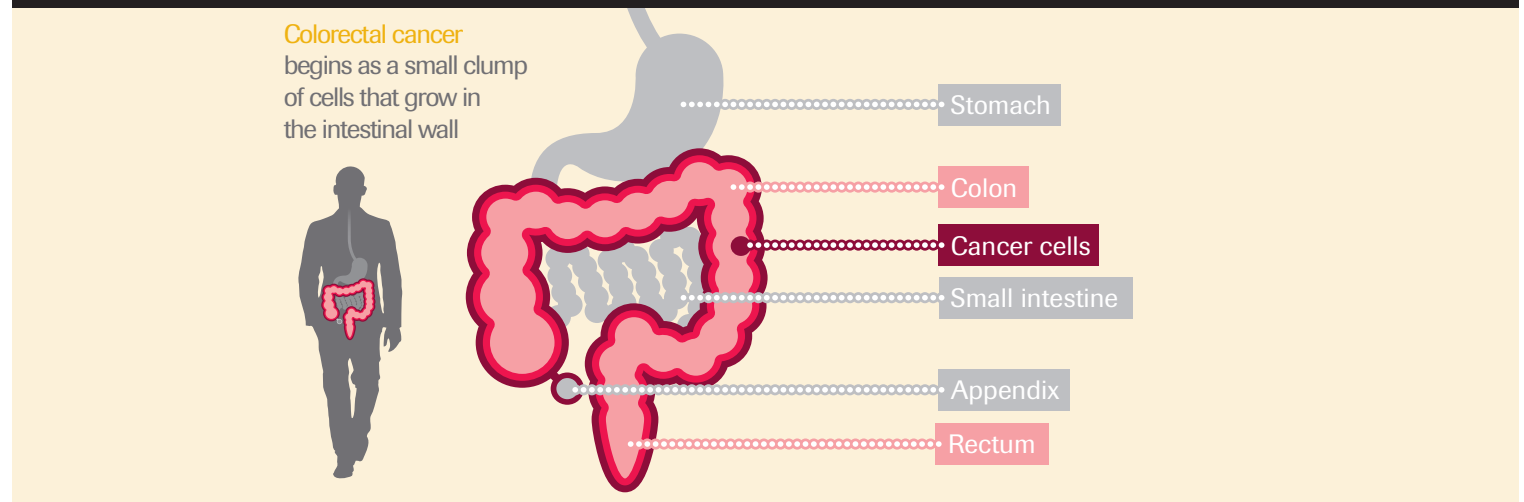
Colorectal cancer is caused by the abnormal growth of epithelial cells which form the lining of the colon or rectum. These small growths (known as polyps) are often benign, although some have the potential to develop and become cancerous. It is estimated that up to two thirds of colorectal polyps are pre-malignant and associated with a risk of colorectal cancer.⁶

Screening and awareness can reduce mortality of colorectal cancer by detecting and removing polyps before they become cancerous, or by discovering the cancer at an earlier stage, where treatment has a higher success rate.⁵ However, there are often no initial symptoms and the cancer may already have spread to other parts of the body by the time the patient is diagnosed.

ii. Causes and risk factors

There are several risk factors that may increase the chance of an individual developing colorectal cancer.

Figure 1 Origins of colorectal cancer



Risk factors:

- **Family history:** A person's risk doubles if a direct relative has previously had the disease. There is an even greater risk if more than one relative has had colorectal cancer.²
- **Genetics:** Individuals with inherited disorders such as familial adenomatous polyposis (FAP), where an individual is prone to polyp formation, have a higher risk of developing colorectal cancer.²
- **Colorectal polyps or inflammatory bowel diseases:** A history of polyps or inflammatory bowel disease, where the bowel is inflamed for many years, increases the risk of colorectal cancer.⁷
- **Age:** Although a person can develop colorectal cancer at any age, the risk increases greatly with age. Over 90% of colorectal cases are diagnosed in patients over the age of 50.⁷
- **Lifestyle:** A sedentary lifestyle is associated with a higher risk of colorectal cancer. Studies have also linked obesity, lack of exercise, smoking and excessive alcohol consumption to a greater risk of colorectal cancer.⁷

Potential protective agents:

- Non-steroidal anti-inflammatory drugs (NSAIDs), such as aspirin, have been associated with a reduced risk of colorectal cancer. A healthy, fibre-containing diet and hormone replacement therapy in women are also possible protective factors.^{8,9}

iii. Symptoms and diagnosis

Early diagnosis of colorectal cancer has the potential to improve survival rates; however early symptoms (such as abdominal pain) may be confused with other diseases,³ meaning many patients have advanced disease when diagnosed.⁴ Almost 85% of patients referred to hospital have one or more of the following high-risk symptoms:¹⁰

- Rectal bleeding
- A mass in the abdomen or rectum
- Change in bowel habit
- Perianal symptoms, such as abscesses or lesions

As the cancer becomes more advanced, other symptoms can develop. For example, excessive bleeding from the colon can cause anaemia, which leaves the patient feeling breathless and tired. If the cancer begins to obstruct the colon, further symptoms include bloating, constipation and vomiting.¹¹

Methods of diagnosis vary from country to country but typically if a patient presents

high-risk symptoms to their doctor they will be given a physical examination. If this raises any concerns, a number of additional tests may be performed:¹²

- Colonoscopy – the entire length of the colon is viewed using a colonoscope.
- Sigmoidoscopy – a small tube (sigmoidoscope) is used to view the lower colon.
- Double contrast barium enema – x-rays of the colon and rectum. Barium lines the colon allowing an outline to be viewed in an x-ray.¹²

A biopsy, where sample tissue is removed during a colonoscopy or sigmoidoscopy, is required to confirm the diagnosis of colorectal cancer and determine how advanced the disease is (staging).¹²

iv. Staging

Staging determines how advanced the cancer is and whether it has spread to other parts of the body. It helps to identify the most appropriate treatment options for the patient. Staging in colorectal cancer can be confirmed by:¹³

- Blood tests to look for tumour markers
- Biopsies, analysing tissue samples taken during a colonoscopy or sigmoidoscopy
- Imaging tests (CT scans, chest x-rays, ultrasound, MRI scans)
- Surgery

The most common staging for colorectal cancer is defined by the tumour, node, metastasis (TNM) staging system, which classes a patient into stages I-IV according to the level of invasion or spread of the tumour to other organs (metastasis).^{14,15}

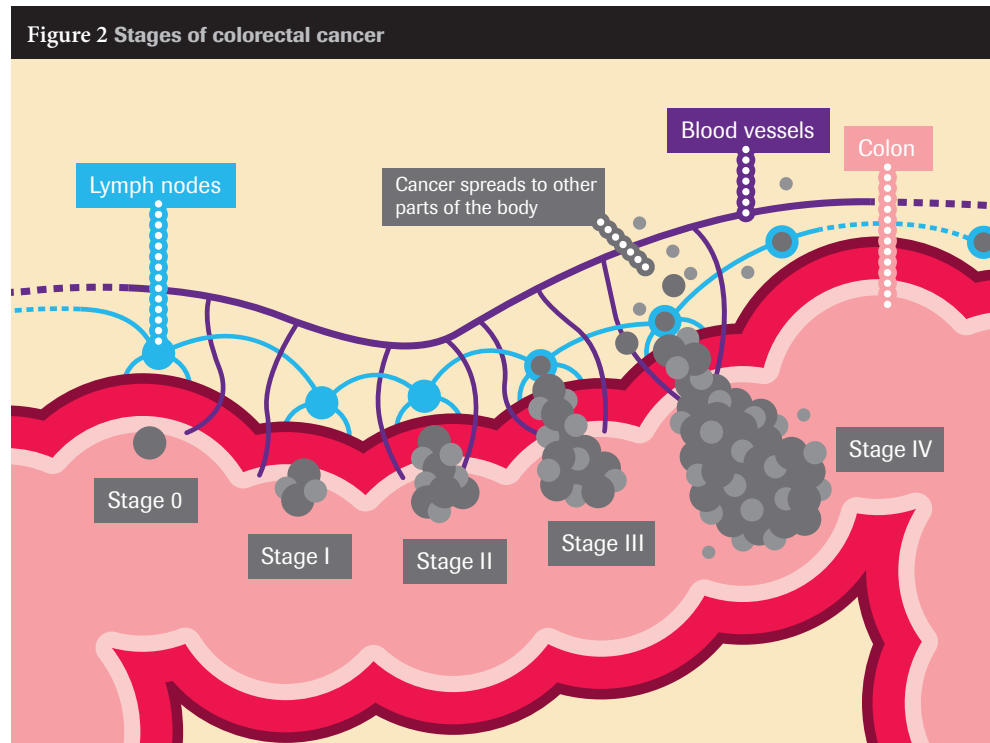
Using the TNM staging, the progression of the original primary tumour is denoted by the letter T (tumour); N (node) indicates whether the tumour has spread to lymph nodes; M (metastasis) represents whether

the tumour has metastasised to distant organs in the body, most commonly the liver or lungs. T, N and M are followed by numbers giving further information on the stage of the disease: increasing numbers signify later stages.¹⁶

Table 1 The stages of colorectal cancer (TNM)^{13,14}

Stage	Classification
Stage I	The tumour is localised to the lining of the colon. T1-T2, N0, M0
Stage II	The tumour grows into the outer lining of the colon or surrounding tissue. T3-T4, N0, M0
Stage III	The cancer has metastasised to the lymph nodes. Any T, N1-N2, M0
Stage IV	The cancer has metastasised to distant organs in the body. Any T, Any N, M1

'Early-stage' disease (stage I and II) describes a tumour that has not yet spread to the lymph nodes or other distant areas in the body. With early-stage disease there is the chance of cure if the tumour can be successfully surgically removed. When cancer spreads from the original site, affecting the lymph nodes (stage III) or other parts of the body (stage IV), treatment becomes more difficult.



Section 2 Epidemiology

i. Incidence & mortality

Worldwide

Colorectal cancer is diagnosed in over 1.2 million people globally each year; it is the second most common cancer in women and the third most common cancer in men. The disease is responsible for approximately

609,000 deaths each year (8% of all cancer deaths),¹ making it the fourth leading cause of cancer death after lung, stomach and liver cancers.

Europe Colorectal cancer is the most common cancer in Europe, with approximately 430,000 new cases each

year;¹ the highest incidence rate of colorectal cancer in the world. It is also the second greatest cause of cancer death in Europe following lung cancer, accounting for 12% of all cancer deaths.

North America There were approximately 177,000 new cases of colorectal cancer

in North America in 2008, making it the second most commonly diagnosed cancer in the region. Colorectal cancer accounted for 11% of all cancer incidence and 9% of all cancer deaths in North America in the same year.¹

Figure 3 Colorectal deaths by region, as a percentage of the incidence of all cancers

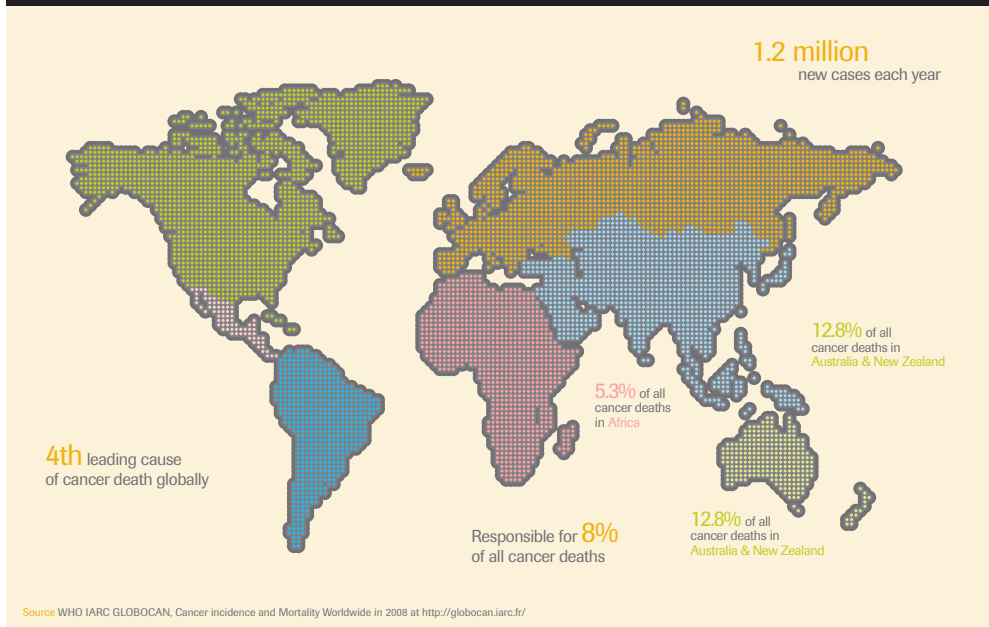
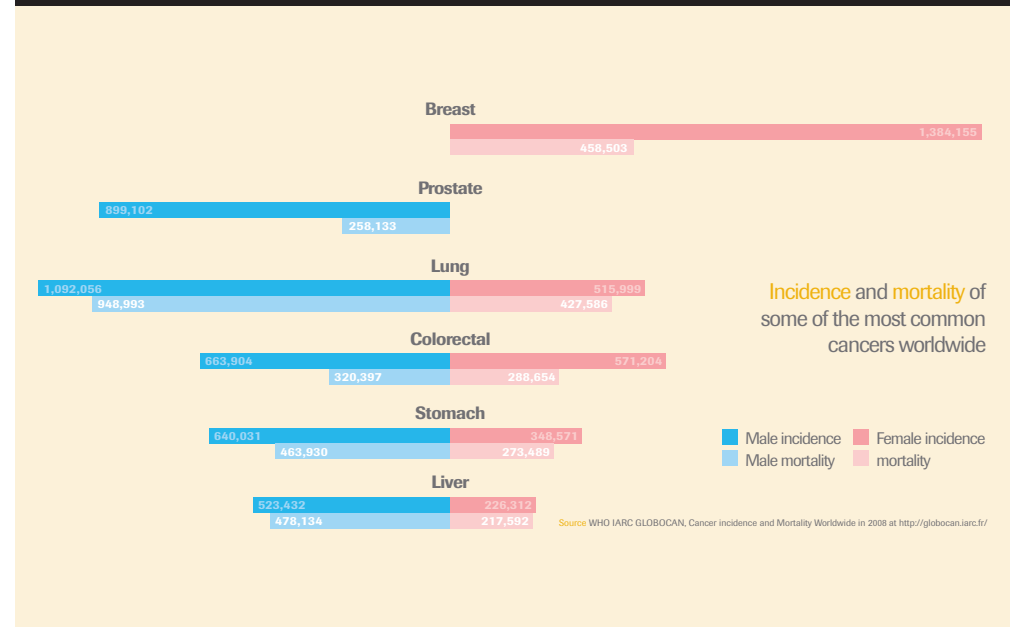


Figure 4 Incidence and mortality of some of the most common cancers worldwide



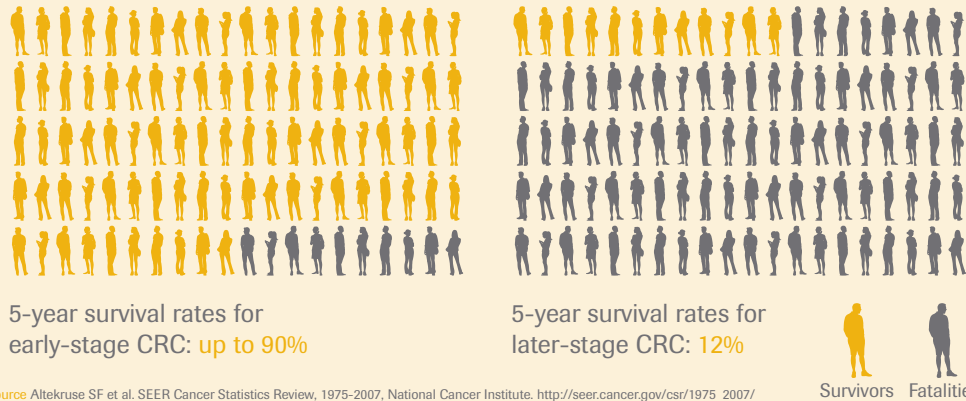
ii. Prognosis

Cancer statistics often use an 'overall 5-year survival rate' to give a better idea of the longer term outlook for people with a particular cancer. The overall 5-year survival rate for colorectal cancer patients is 65%,¹⁷ although this differs greatly depending on how advanced the cancer is.

The 5-year survival rate for a patient diagnosed with stage I or II colorectal cancer, where the tumour is localised to the colon, is up to 90%. Approximately two fifths of patients are diagnosed at this stage. However the 5-year survival rate for patients diagnosed with stage IV disease, once the cancer has metastasised to other organs, is only 12%.¹⁷

Figure 5 Incidence and mortality of some of the most common cancers worldwide

Colorectal cancer average 5-year survival rate depending on stage of diagnosis



Section 3

Treatment

Treatment options for patients vary and are assessed taking into account the following variables:

- Tumour size
- Stage of diagnosis
- The location of the tumour in the colon or rectum
- The risk of the cancer returning
- The physical health of the patient

In general the current treatment options for colorectal cancer are surgery, chemotherapy, and biological therapies. Radiotherapy is not often used to treat metastatic colorectal cancer due to side-effects, although it can be used after surgery to destroy any residual cancer cells.¹⁸

i. Surgery

The majority of patients with early-stage colorectal cancer will undergo surgery to remove as much of the tumour as possible in a procedure known as 'resection'. Any areas surrounding the cancerous tissue and nearby lymph nodes will also be removed to reduce the risk of the cancer spreading. Resection is also a treatment option for some patients with later stage disease, particularly when the cancer has metastasised to the liver. A less invasive procedure known as laparoscopic resection, where the affected area of the colon is removed through keyhole surgery, can also be performed on patients with early-stage colorectal cancer.¹⁹

ii. Chemotherapy

Patients diagnosed with advanced disease are usually treated with chemotherapy after surgery, known as 'first-line' treatment. This involves a combination of a fluoropyrimidine and most often fluorouracil (5-FU) with leucovorin (folinic acid or LV) and oxaliplatin, known as FOLFOX¹⁹ or with irinotecan, known as FOLFIRI.

Some patients with advanced colorectal cancer who are not initially able to undergo surgery due to invasive tumours can be treated with chemotherapy before being considered for surgery (called neoadjuvant treatment).²⁰

Many people with colorectal cancer initially respond to chemotherapy, but

unfortunately, in the majority of cases the disease eventually progresses after first-line treatment. When this occurs the patient may undergo another round of chemotherapy, known as 'second-line' treatment. Detecting disease recurrence early is important in improving survival as unfortunately 30%-50% of patients will eventually die from the disease, so patients are routinely checked after completing the chemotherapy regimen.^{19,21}

iii. Biological therapies

Several types of biological therapy are available to treat metastatic colorectal cancer including anti-angiogenics and the Epidermal Growth Factor Receptor (EGFR) inhibitors. Biological therapies are typically given in combination with chemotherapy.

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