

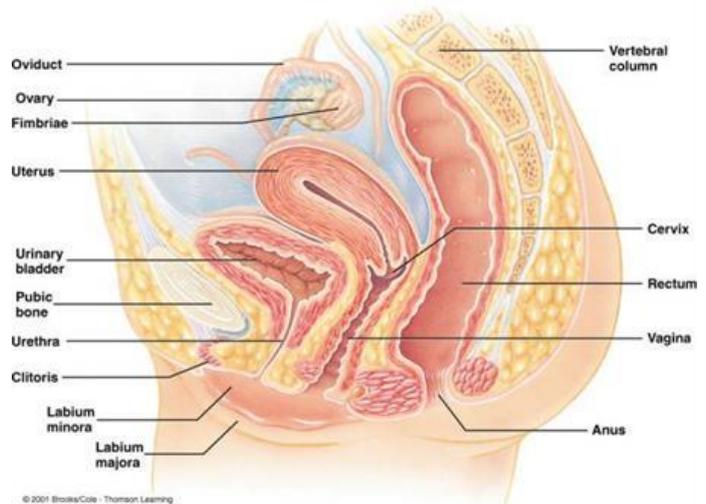


## Fact Sheet on Cancer of the Anus

### Introduction

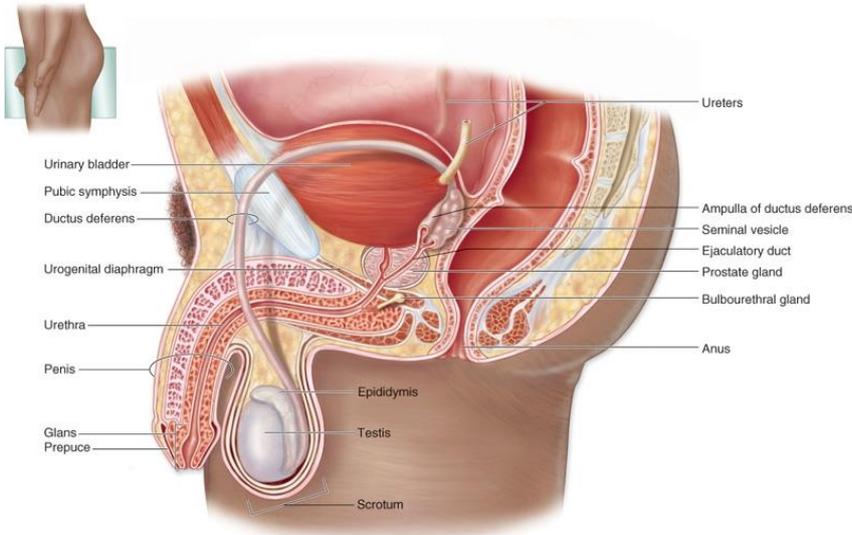
The human anus (from Latin *anūs* meaning 'ring', 'circle') is the external opening of the rectum. Like other vertebrates, its closure is controlled by sphincter muscles. Faeces are expelled from the body through the anus during the act of defaecation, the primary function of the anus.

[Picture Credit: Female Pelvis]



The anus is often considered a taboo part of the body, however, the anus is also the site of potential infections and other conditions, including cancer and, therefore, of great medical concern (Wikipedia).

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[Picture Credit: Male Pelvis]

The anus starts at the bottom of the rectum, the last portion of the colon (large intestine). The ano-rectal line separates the anus from the rectum. Tough tissue called fascia surrounds the anus and attaches it to nearby structures.

Circular muscles called the external *sphincter ani* form the wall of the anus and hold it closed. Glands release fluid

into the anus to keep its surface moist.

A plate-like band of muscles, called the *levator ani* muscles, surround the anus and form the floor of the pelvis. A network of veins lines the skin of the anus.

### Anal Cancer

Anal cancer is an uncommon malignancy that starts in the anus - the opening at the end of the rectum. When it is found early, anal cancer is highly treatable.

**Nelson, V.M. & Benson, A.B. 3<sup>rd</sup>.** 2017. Epidemiology of anal canal cancer. *Surg Oncol Clin N Am.* 2017 Jan;26(1):9-15. doi: 10.1016/j.soc.2016.07.001.

“Anal cancer is a rare malignancy, although its incidence has been increasing in recent decades.”

### Incidence of Anal Cancer in South Africa

According to the outdated National Cancer Registry (2017), known for under reporting, the following number of anal cancer cases was histologically diagnosed in South Africa during 2017:

Group - Males 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All males	128	1:1 525	0,32%
Asian males	4	1:1 248	0,41%
Black males	84	1:1 706	0,61%
Coloured males	13	1:1 013	0,28%
White males	27	1:1 415	0,12%

Group - Females 2017	Actual No of Cases	Estimated Lifetime Risk	Percentage of All Cancers
All females	170	1:1 613	0,41%
Asian females	4	1: 2 189	0,31%
Black females	124	1:1 804	0,65%
Coloured females	9	1:2 671	0,20%
White females	33	1:1 085	0,18%

The frequency of histologically diagnosed cases of anal cancer in South Africa for 2017 was as follows (National Cancer Registry, 2017):

Group - Males 2017	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	0	1	16	31	34	28	10	8
Asian males	0	0	1	0	0	2	1	0
Black males	0	1	14	27	23	12	5	2
Coloured males	0	0	0	2	3	6	2	0
White males	0	0	1	2	8	8	2	6

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Group - Females 2017	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	1	8	39	47	28	27	15	5
Asian females	0	0	1	1	1	1	0	0
Black females	1	8	35	40	22	11	6	1
Coloured females	0	0	3	1	0	3	1	1
White females	0	0	0	5	5	12	8	3

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

According to **Bruni, et al.**, (2019), the burden of cancer of the anus for South Africa for 2018 is estimated as (based on Globocan estimates):

- Annual number of cancer of the anus cases 244
- Annual number of cancer of the anus deaths 118

### Risk Factors for Anal Cancer

Several factors have been found to increase the risk for anal cancer, including:

- older age – most cases of anal cancer occur in people aged 50 and older
- many sexual partners – men and women who have many sexual partners over their lifetimes have a greater risk for anal cancer
- unprotected anal sex – men and women who engage in unprotected anal sex have an increased risk for anal cancer
- smoking – smoking may increase the risk for anal cancer. Former smokers have only a slightly elevated risk for anal cancer
- human papillomavirus (HPV) – HPV infection increases the risk for several cancers, including anal cancer and cervical cancer. HPV infection is a sexually transmitted infection that can also cause genital warts. HPV may cause cells in the anal canal to appear abnormal – a condition called anal squamous intraepithelial lesions (ASIL). The abnormal cells associated with ASIL are not cancer but it may develop into anal cancer, however, some people with ASIL never develop anal cancer

**Staples, J.N. & Duska, L.R.** 2019.

“The human papilloma virus vaccination should be offered to all girls and boys aged 11 to 12 years, and can also be given as early as age 9 and through 26 years of age.”

- 95% of anal cancers are caused by the human papillomavirus (HPV). There are many types of HPV. Some HPV types cause benign warts, but some cause lesions (also called dysplasia) that can progress to invasive cancer. HPV-16 and HPV-18 are the high-risk strains responsible for the majority of HPV-associated cancers.
- drugs or conditions that suppress the immune system – people who take drugs to suppress their immune system (immunosuppressive drugs), including people who have received organ transplants may have an increased risk for anal cancer. Long-term use of corticosteroids, such as those prescribed to control autoimmune disorders also may increase the risk for anal cancer. HIV (the virus that causes AIDS) suppresses the immune system and increases the risk for anal cancer
- fistulas – presence of abnormal openings in or around the anus
- history of cervical, vaginal or vulval cancer – some studies show that women who had cervical, vulval or vaginal cancer have a higher risk of developing abnormal cells in the anus or anal cancer

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than the general population. The risk is also increased for women with a history of abnormal cells in the cervix (cervical intraepithelial neoplasia), vulva (vulval intraepithelial neoplasia) or vagina (vaginal intraepithelial neoplasia).

**Valvo, F., Ciurlia, E., Ayuzzi, B., Doci, R., Ducreaus, M., Roelofsen, F., Roght, A., Trama, A., Wittekind, C. & Bosset, J-F. 2019.**

“Anal canal accounts for 2% of all cancer and its incidence increases with age with a predominance in woman. About 80% of all primary anal canal cancers are squamous; adenocarcinoma arising from the glands or glandular ducts shows a behaviour that is similar to that of the adenocarcinoma of the rectum. Risk factors includes sexually transmitted infection with Human Papillomavirus, cigarette smoking, immunosuppression, and sexual practices. The standard treatment for anal canal is chemo - radiation with a combination of fluoropyrimidines and mitomycin or cisplatin. Salvage surgery may be necessary for residual disease after radiotherapy or chemoradiation, for locoregional relapse and/or for sequelae. In the metastatic setting a multidisciplinary approach is preferred and includes medical treatment, surgery, and RT, if appropriate. Discussing these possible options in the initial stage is of most importance to ensure the best quality of life (QoL) for patients.”

### **Screening for Anal Cancer**

Ongoing research is being done on the value of screening tests for anal cancer, especially in people with major risk factors. The test studied most is anal cytology, sometimes called the *anal Pap test*. This test may be useful in early diagnosis of anal cancer and pre-cancer (called *anal intraepithelial neoplasia*, or AIN).

In this test, cells are gently scraped from the lining layer of the anus and checked under a microscope. Some doctors already recommend this test for people at high risk for anal cancers, such as those who are HIV positive.

Research is also in progress on treating AIN to help prevent cancer from developing.

### **Signs and Symptoms of Anal Cancer**

Signs and symptoms of anal cancer include:

- rectal bleeding - the patient may notice blood on faeces or toilet paper
- pain in the anal area
- lumps around the anus. These are frequently mistaken for piles (haemorrhoids)
- mucus discharge from the anus
- jelly-like discharge from the anus
- anal itching
- change in bowel movements. This may include diarrhoea, constipation, or thinning of stools
- faecal incontinence (problems controlling bowel movements)
- bloating
- women may experience lower back pain as the tumour exerts pressure on the vagina
- women may experience vaginal dryness

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- a sense of fullness and constant need to go to the bathroom, or both, which may occur as tumours grow and begin to invade the sphincter muscle
- change in the diameter of stool
- swollen lymph nodes in the anal or groin areas
- ulcers around the anus that can spread to the skin of the buttocks

### Diagnosis of Anal Cancer

Anal cancer is often fairly easy to diagnose because it is in a fairly easy-to-reach area. Some cases of anal cancer in people at high risk for that disease are diagnosed by screening tests, such as the digital rectal exam and/or anal Pap test, but most people are diagnosed after their cancer starts to cause symptoms.

**Young, A.N., Jacob, E., Willauer, P., Smucker, L., Monzon, R. & Ocegüera, L. 2020.**

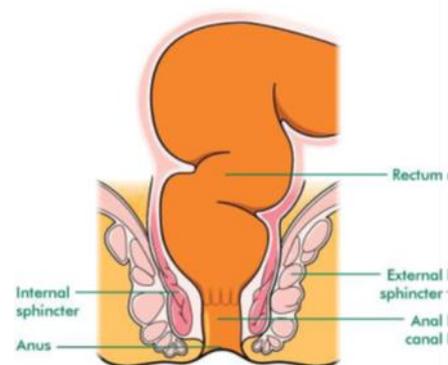
“Anal cancer is a rare cancer, comprising less than 5% of gastrointestinal tract malignancies. Diagnosis of anal canal cancer can be difficult given that presenting symptoms are similar to those of benign anorectal diseases. General surgeons who encounter suspected anal canal cancer need to have a good understanding of the anatomy of the anal canal, high index of suspicion for malignancy, and low threshold to biopsy lesions when indicated. This article discusses the most commonly encountered anal canal tumors, the evaluation of these tumors, and their management. The foundation for successful therapy includes timely diagnosis, accurate staging, and routine surveillance.”

### Types of Anal Cancer

About 80% anal cancers are squamous cell cancers, sometimes called epidermoid cancers. There are 3 types of squamous cell anal cancer, namely:

- large cell keratinising cancer
- large cell non keratinising (also called transitional) cancer
- basaloid cancer

[Picture Credit: Anal Canal]



A keratinising cancer has keratin (the protein that forms one’s hair and nails) in the cancer cells. This type of anal cancer starts in the lower part of the anus. Non-keratinising types start from the transitional zone of the anal canal, where the squamous cells meet the glandular cells. Many anal cancers will have a mix of these cell types. All these squamous cell types of anal cancer are treated in the same way.

### Non-epidermoid cancer

The other 2 out of 10 anal cancers (20%) are:

- adenocarcinoma - this is a rare type of anal cancer that affects the glandular cells that produce mucus in the anal canal. Only 5% of anal cancers are this type. This type of anal cancer is treated in the same way as rectal cancer
- small cell cancers - small cell carcinoma affecting the anal canal is a rare and poorly understood entity which can, in its early stages, masquerade as benign cells
- undifferentiated cancers - undifferentiated cells are cells that have become so abnormal that often we cannot tell what types of cells they started from
- basal cell carcinoma - This is a type of skin cancer and it develops in the area around the anus. You can find information about treatment of basal cell cancers in the skin cancer section
- melanomas - this is another type of skin cancer. These cancers develop from the cells that produce melanin, the pigment or colour for the skin. Treatment is the same as for other melanomas

This group is known as non-epidermoid cancers. They behave differently to squamous cell anal cancers, so the treatment is different.

Cancers that start at the anal margin, usually look more like normal cells (they are well differentiated). Anal margin tumours are more common in men than women. Cancers that start higher up in the anal canal are more common in women.

### **Lowering the Risk for Anal Cancer**

Since the cause of many cases of anal cancer is unknown it is not possible to prevent this disease completely.

The best way to reduce the risk of developing anal cancer is to avoid infection with HPV or HIV. The risk of these infections is higher for those who have sex with multiple partners and those who have unprotected anal sex (American Cancer Society).

- always use a condom - wearing a condom may provide protection against HPV. HPV is a virus transmitted through sexual contact that is linked to several types of cancer
- limit the number of sexual partners - when a person has multiple sexual partners they are at an increased risk for both HPV and anal cancer
- avoid unprotected anal intercourse – unprotected anal intercourse increases the risk factor for anal cancer for both men and women
- quit smoking and/or using other tobacco products - smokers are 4 times more likely to develop anal cancer than non-smokers. Smoking puts individuals at a higher risk for many other types of cancer as well like lung cancer
- avoid sex with people with sexually transmitted infections (STI) or those who have or have had multiple sexual partners
- get an HPV vaccine - Gardasil® and Cervarix® help protect against certain types of HPV. Individuals who already have HPV will not be cured by having these vaccines

### **Staging of Anal Cancer**

Staging is the process of finding out how far a cancer has spread. This is important because treatment options and outlook for recovery and survival depend on the cancer's stage.

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Staging of anal cancer uses a system created by the American Joint Committee on Cancer (AJCC). The staging description that follows applies only to tumours in the anal canal, not to cancers that involve only the anal margin or perianal skin.

### **The TNM system**

The *TNM system* for staging contains 3 key pieces of information:

- **T** describes the size of the primary tumour, measured in centimetres (cm), and whether the cancer has spread to organs next to the tumour
- **N** describes the extent of spread to nearby (regional) lymph nodes
- **M** indicates whether the cancer has metastasised (spread) to other organs of the body

**Maas, M., Tielbeek, J.A.W. & Stoker, J. 2020.**

“Anal cancer is a relatively rare malignancy. Treatment consists of chemoradiation and most patients achieve a complete response. Local evaluation of the T and N stage is performed by MR imaging. Whole-body staging with 18F-fluorodesoxyglucose positron emission tomography computed tomography scans or computed tomography scans is used to detect metastases. T stage is based on tumor size or invasion of organs. N stage is based on nodal location. After chemoradiation, clinical evaluation and MR imaging is used to assess tumor and nodal response. Maximal response is achieved 6 months after chemoradiation. Beware of development of anal cancer in perianal fistulas.”

### **Spread of Cancer of the Anus**

Cancer from the anus metastasises (spreads) mostly to:

- lymph nodes of your abdomen, it may cause bloating, a swollen abdomen, loss of appetite, or a feeling of fullness
- the liver, it may cause pain on the upper right side of your abdomen, bloating, loss of appetite, or a feeling of fullness
- the lungs, it may cause you to cough, spit up blood, or have a hard time breathing
- the bones, it may cause bone pain, especially in your back, hips, and pelvis
- the brain, it may cause problems with memory, concentration, balance, or movement

### **Prognosis (Outlook)**

As with many types of cancer, the outcome of anal cancer depends on how advanced it is when diagnosed - in other words, the stage of the cancer. Because anal cancer is rare, it is harder to draw conclusions from the statistics because they are based on a small number of people. Generally the outlook is much better for people with anal cancer compared to many other types of cancer.

Overall, between 60% and 75% of people with anal cancer will live for at least 5 years. For people diagnosed with stage 1 and 2 anal cancer more than 80% will live for at least 5 years.

In those whose cancer has spread to the lymph nodes or nearby body structures, such as the bladder (stage 3), between 60% to 80% will live for at least 5 years.

Unfortunately the outlook is much poorer if the cancer has spread to distant organs (stage 4). In this situation, only about 10% will live for at least 5 years.

### **Treatment of Anal Cancer**

Most patients with anal cancer can have their cancer treated successfully with a combination of external beam radiation therapy and anticancer drugs known as chemotherapy.

Preserving function of the anal sphincter muscles (ring-shaped muscles surrounding the opening) is one potential advantage of using a combination of therapies.

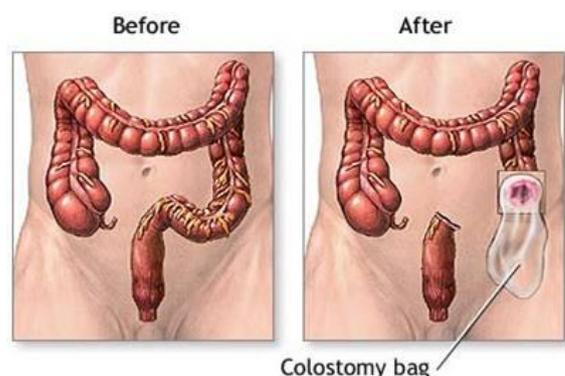
Chemotherapy - chemotherapy is drug treatment to kill cancer cells. Some chemotherapy drugs work because they kill any rapidly dividing cells, and many cancer cells grow and multiply more rapidly than normal cells. Other chemotherapy drugs attack cancer cells by targeting specific differences between cancer cells and normal cells (targeted therapies).

Radiation therapy - the goal of radiation therapy is to destroy cancer cells while minimising the damage to surrounding tissue. An external beam therapy known as intensity modulated radiation therapy (IMRT) uses precisely shaped radiation beams to accurately deliver high-dose treatment. IMRT yields positive outcomes with fewer side effects than older forms of external radiation therapy.

Intraoperative radiation therapy - (IORT) delivers a concentrated beam of radiation to cancerous tumours while they are exposed during surgery. This technique allows doctors to administer high doses of radiation to tumours while sparing nearby healthy organs from radiation. IORT is still considered experimental in the treatment of anal cancer.

Surgery - surgical removal of the cancer is performed only when radiation and chemotherapy are not completely effective. Surgery may be used to treat small anal tumours or be used in combination with chemotherapy or radiotherapy for advanced anal cancer. Surgeons use several techniques to remove the cancer.

[Picture Credit: Colostomy Following Resection of Anus]



The surgeon may remove the cancer and a small amount of adjacent healthy tissue (local resection). This procedure can often be used when doctors diagnose the cancer early. If more extensive surgery is needed, an abdominoperineal resection (APR) may be done. During this procedure, the surgeon

ADAM.

removes the anus and the lower part of the rectum and creates an opening (stoma) on the outside of the body to pass waste. This is known as a colostomy.

**Katsuno, H., Hanai, T., Masumori, K., Koide, Y., Ashida, K., Matsuoka, H., Tajima, Y., Endo, T., Mizuno, M., Cheong, Y., Maeda, K. & Uyama, I. 2020.**

“The number of patients undergoing robotic surgery for rectal cancer has rapidly increased in Japan, since the government approved the procedure for national insurance coverage in April 2018. Robotic surgery has the potential to overcome some limitations of laparoscopic surgery, especially in the narrow pelvis, providing a three-dimensional view, articulated instruments, and a stable camera platform. Although meta-analyses and randomized controlled trials have failed to demonstrate the superiority of robotic surgery over laparoscopic surgery with respect to the short-term clinical outcomes, the published findings suggest that robotic surgery may be potentially beneficial for patients who are obese, male, or patients undergoing sphincter-preserving surgery for rectal cancer. The safety and feasibility of robotic surgery for lateral lymph node dissection, the standard procedure for locally advanced lower rectal cancer in Japan, have been demonstrated in some retrospective studies. However, additional prospective, randomized trials are required to determine the actual benefits of robotic surgery to ameliorate the urogenital and oncological outcomes. The cost of this approach is a long-standing principal concern. A literature search showed that the cost of robotic surgery for rectal cancer was 1.3-2.5 times higher per patient than that for the laparoscopic approach. We herein describe our surgical technique using a da Vinci Surgical System (S/Si/Xi) with 10 years of experience in performing robotic surgery. We also review current evidence regarding short-term clinical and long-term oncological outcomes, lateral lymph node dissection, and the cost of the procedure.”

#### Immunotherapy

**Phuong, L. & Rajdev, L. 2020.**

**Purpose of review:** Standard treatment for early-stage squamous cell cancer of the anal canal (SCCA) includes concurrent chemotherapy and radiation to achieve curative intent. Treatment options are limited, however, especially with locoregional disease relapse occurring in 20-30% of patients and about 10-30% of patients presenting with metastatic disease. With more than 90% of SCCAs occurring in the setting of HPV, immune-based therapies are now the target of possible new treatments for this rare disease. This review highlights the role of immunotherapy in HPV-associated SCCA.

**Recent findings:** Immunotherapy has been shown to extend progression-free survival and overall survival in various solid malignancies, including SCCA. So far, single-agent monotherapy with either nivolumab or pembrolizumab has shown durable clinical response with a tolerable side effect profile. The 2018 NCCN guidelines now advise nivolumab or pembrolizumab monotherapy as second-line treatment in the management of metastatic SCCA. Further investigation with immunotherapy continues to be critical for such a rare malignancy with few treatment options.

#### **Lifestyle Changes Following a Diagnosis of Anal Cancer**

In the event of a patient having had a colostomy, several lifestyle changes will be required. Please refer to CANSA’s Fact Sheet on Colorectal Cancer for additional information on colostomy and colostomy care.

## About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The [South African National Clinical Trials Register](#) provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: [www.sanctr.gov.za/](http://www.sanctr.gov.za/)

## Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst CANSA has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.



## Sources and References Consulted or Utilised

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<http://cancer.about.com/od/analcancer/a/analcancerpreve.htm>

### American Cancer Society

<http://www.cancer.org/cancer/analcancer/detailedguide/anal-cancer-diagnosis>

<http://www.cancer.org/cancer/analcancer/detailedguide/anal-cancer-prevention>

<http://www.cancer.org/cancer/analcancer/detailedguide/anal-cancer-staging>

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### **Anal Canal**

[http://www.macmillan.org.uk/Cancerinformation/Cancertypes/Anal/Analcancer.aspx#DynamicJumpMenuManager\\_6\\_Ancor\\_1](http://www.macmillan.org.uk/Cancerinformation/Cancertypes/Anal/Analcancer.aspx#DynamicJumpMenuManager_6_Ancor_1)

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### **Cancer.Net**

<http://www.cancer.net/cancer-types/anal-cancer>

### **Cancer Research UK**

<http://www.cancerresearchuk.org/cancer-help/type/anal-cancer/about/risks-and-causes-of-anal-cancer>

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<http://www.cancerresearchuk.org/cancer-help/type/anal-cancer/treatment/statistics-and-outlook-for-cancer-of-the-anus>

### **Caring4Cancer**

<https://www.caring4cancer.com/go/anal/basics/what-are-the-signs-and-symptoms-of-anal-cancer.htm>

### **Colostomy Following Resection of Anus**

<http://www.bing.com/images/search?q=free+pics+colostomy+&view=detail&id=24FFA3D2379A7C54DB00FFD52EAFD94247D51F4C&first=31&FORM=IDFRIR>

**Durot, C., Dohan, A., Boudiaf, M., Servois, V., Sover, P. & Hoeffel, C.** 2017. Cancer of the anal canal: diagnosis, staging and follow-up with MRI. *Korean J Radiol*. 2017 Nov-Dec;18(6):946-956. doi: 10.3348/kjr.2017.18.6.946. Epub 2017 Sep 21.

### **Female Pelvis**

<http://www.bing.com/images/search?q=free+pics+pelvis+male+female&view=detail&id=DBCEE4762759C34AC7332FA508C4E0DD736D23F0&first=241&FORM=IDFRIR>

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**Maas, M., Tielbeek, J.A.W. & Stoker, J.** 2020. Staging of anal cancer: role of MR imaging. *Magn Reson Imaging Clin N Am*. 2020 Feb;28(1):127-140.

### **MacMillan Cancer Support**

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### **Male Pelvis**

<http://2kfans.com/unik/male-reproductive-system-diagram-patient.html>

### **Mayo Clinic**

<http://www.mayoclinic.com/health/anal-cancer/DS00852/DSECTION=symptomshttp://www.mayoclinic.com/health/anal-cancer/DS00852/DSECTION=risk-factors>

<http://www.mayoclinic.com/health/anal-cancer/DS00852/DSECTION=prevention>

<http://www.mayoclinic.org/anal-cancer/treatment.html>

### **MD Anderson Cancer Center**

<http://www.mdanderson.org/patient-and-cancer-information/cancer-information/cancer-types/anal-cancer/prevention/index.html>

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**Medical News Today**

<http://www.medicalnewstoday.com/articles/156549.php>

**National Cancer Institute**

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