

Cancer Association of South Africa (CANSA)



CANSA Fact Sheet on Melanoma of the Vulva and Vagina

Introduction

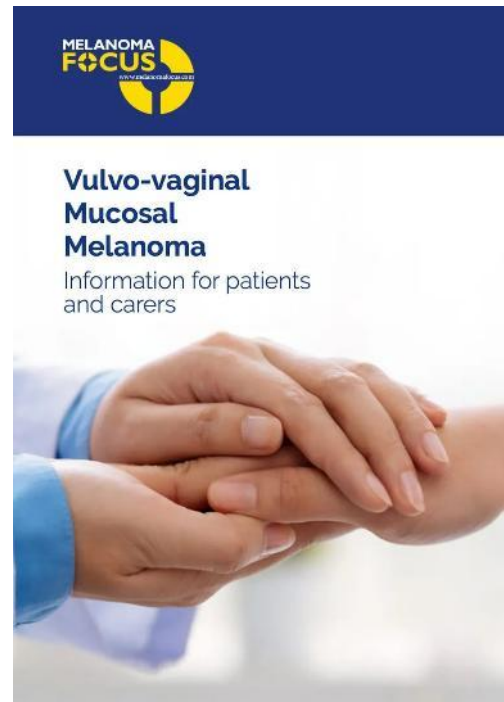
The vagina or birth canal is the opening through which menstrual fluid leaves a woman's body and babies are born. It is connected to the cervix, which is the opening of the uterus or womb, and the vulva (folds of skin around its opening).

Usually, the vagina is in a collapsed position with its walls touching. The walls have many folds that allow the vagina to open and expand during sexual intercourse and vaginal childbirth. The vaginal lining is kept moist by mucus released from glands in the cervix.

[Picture Credit: Melanoma of the Female Genitalia]

The vaginal walls have a thin layer of cells called the epithelium, which contains cells called squamous epithelial cells. The vaginal wall, underneath the epithelium, is made up of connective tissue, involuntary muscle tissue, lymph vessels, and nerves.

Melanoma is a cancer that starts in cells called melanocytes. Melanocytes are pigment producing cells. They are mostly found in the skin. Most melanomas develop in parts of the body that are exposed to the sun. But one can get them anywhere, including in body organs, because there are melanocytes in those areas too. That is why one sometimes hears melanoma of the skin called cutaneous melanoma or melanoma of the skin. Cutaneous means of the skin. It is still not clear why melanomas can form in parts of the body that are not exposed to the sun.



Even though some melanomas grow in parts of the body that is not exposed to the sun, it is still very important to remember that the best way to keep one's risk of melanoma or other skin cancers as low as possible is to avoid being in the sun too much.

If someone has melanoma in an unusual site such as genital skin, the treatment should be planned by a multidisciplinary team (MDT). The team should include skin melanoma specialists and surgeons and oncologists who normally treat genital cancer.

In this Fact Sheet melanoma of the vagina and vulva will be discussed together under the heading of cancer of the vagina.

It is not clear what causes vaginal cancers. In general, cancer begins when healthy cells acquire a genetic mutation that turns normal cells into abnormal cells.

Healthy cells grow and multiply at a set rate, eventually dying at a set time. Cancer cells, however, grow and multiply out of control, and they do not die. The accumulating abnormal cells form a mass (tumour).

Cancer cells invade nearby tissues and can break off from an initial tumour to spread elsewhere in the body (metastasis).

Vaginal cancer is divided into different types based on the type of cell where the cancer began.

Vaginal cancer types include:

- Vaginal squamous cell carcinoma, which begins in the thin, flat cells (squamous cells) that line the surface of the vagina, is the most common type
- Vaginal adenocarcinoma, which begins in the glandular cells on the surface of your vagina
- Vaginal melanoma, which develops in the pigment-producing cells (melanocytes) of your vagina
- Vaginal sarcoma, which develops in the connective tissue cells or muscle cells in the walls of your vagina
- Clear cell adenocarcinoma, which occurs in women whose mothers took the drug diethylstilbestrol (DES) during pregnancy between the late 1940s and 1971. It is estimated that one woman out of 1 000 women exposed to DES will develop vaginal cancer.

(Cancer Research UK, 2025; Melanoma Focus, 2026).

Duffau, K., Zheng, G., Munk, C., Sundström, K., Wang, J., Baandrup, L., Hædersdal, M. & Kjær, S.K. 2025.

Objectives: Vulvar malignant melanoma (VuMM) represents a rare malignancy. This study examines and compares the incidence and trends in incidence of VuMM in Denmark and in Sweden over a period of >40 years.

Study design: A nationwide, population-based registry study conducted in two countries.

Main outcome measures: We identified incident VuMM cases in the Danish and Swedish Cancer Registries. Information on age at diagnosis, anatomical site, histology, and stage of disease was retrieved. We calculated age-specific and age-standardized incidence rates (ASRs) with temporal

trends in incidence evaluated by estimated annual percent change (EAPC) with 95 % confidence intervals (CI).

Results: A total of 524 women with VuMM, encompassing 171 women in Denmark (1978-2022) and 353 women in Sweden (1978-2018), were included. The age-specific incidence rates increased with age throughout the study period in both countries. The ASR decreased in both countries: in Denmark, from 1.03 (95 % CI: 0.59-1.48) per 1,000,000 to 0.55 (95 % CI: 0.26-0.83); and in Sweden from 1.25 (95 % CI: 0.22-2.28) to 0.76 (95 % CI: 0.42-0.84). This corresponded to EAPCs of -1.65 (95 % CI: -2.45; -0.84) in Denmark and -1.22 (95 % CI: -1.69; -0.75) in Sweden.

Conclusions: The age-standardized and age-specific VuMM incidence rates were nearly identical in Denmark and Sweden, which are countries with similar demographic characteristics, and a free-of-charge healthcare system. The incidence of VuMM showed an equal and statistically significant decrease in Denmark and Sweden during the last four decades. The explanation for the decrease is currently unknown.

Conflict of interest statement

Declaration of competing interest MH reports receiving research grants from Leo Pharma and L'Oréal/La Roche-Posay, consulting fees from L'Oréal/La Roche-Posay and Procter & Gamble, payment for lectures from Galderma, as well as equipment from Cynosure-Lutronic, GME Medical and Venus Concept within the last 36 months. None of these has been given in relation to the work of the present study. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Nogueira-Rodrigues, A., Oonk, M.H.M., Lorusso, D., Slomovitz, B., Leitão, M.M. J. & Baiocchi, G. 2025.

“Vulvar and vaginal cancers represent rare malignancies, with an incidence of 2.7 per 100,000 women for vulvar cancer, predominantly affecting women older than 60 years, although rising rates are observed in younger demographics. Approximately 90% of vulvar cancers are squamous cell carcinoma and frequently are associated with human papillomavirus (HPV) infection. Vaginal cancer, constituting less than 1% of all female cancers, similarly exhibit HPV-related trends. This review delineates the etiology, histopathology, and treatment strategies for carcinomas and vulvovaginal melanomas and sarcomas. Surgical intervention remains the primary treatment modality for vulvar cancer, involving tumor resection and inguinofemoral lymph node staging. For locally advanced vulvar carcinoma, chemoradiation is advised when exenterative surgery would be indicated. Recurrence rates within 2 years after diagnosis range from 12% to 37%. Unfortunately, systemic treatments for recurrent or metastatic disease are limited, with 5-year survival rates at approximately 20%. Current evidence primarily derives from retrospective studies or small phase 2 trials or otherwise is extrapolated from the treatment of cervical cancer. Enrollment in clinical trials is strongly advocated, along with prompt access to best supportive care to mitigate the effect of locoregional progression on quality of life. Moreover, the psychosocial implications of treatment on body image and sexuality necessitate careful consideration. Future HPV vaccination initiatives may reduce cancer incidence, although significant effects of such vaccination will manifest over decades, underscoring the urgent need to enhance treatment efficacy and minimize morbidity in vulvar and vaginal cancers.”

The International Classification of Disease 10th Version (ICD-10)

The International Classification of Diseases (ICD) is designed to promote international comparability in the collection, processing, classification, and presentation of mortality statistics. This includes providing a format for reporting causes of death on the death certificate.

ICD serves a broad range of uses globally and provides critical knowledge on the extent, causes and consequences of human disease and death worldwide via data that is reported and coded with the ICD. Clinical terms coded with ICD are the main basis for health recording and statistics on disease in primary, secondary and tertiary care, as well as on cause of death certificates. These data and statistics support payment systems, service planning, administration of quality and safety, and health services research. Diagnostic guidance linked to categories of ICD also standardizes data collection and enables large scale research.

For more than a century, the International Classification of Diseases (ICD) has been the basis for comparable statistics on causes of mortality and morbidity between places and over time. Originating in the 19th century, the latest version of the ICD, ICD-11, was adopted by the 72nd World Health Assembly in 2019 and came into effect on 1st January 2022.

The ICD-10 Code for malignant melanoma female genitalia – C51.9.
(World Health Organization, 2025)

Tumour Grade vs Tumour Stage

A cancer's grade describes how abnormal the cancer cells and tissue look under a microscope when compared to healthy cells. Cancer cells that look and organise most like healthy cells and tissue are low grade tumours. Doctors describe these cancers as being well differentiated. Lower grade cancers are typically less aggressive and have a better prognosis.

While a grade describes the appearance of cancer cells and tissue, a cancer's stage explains how large the primary tumour is and how far the cancer has spread in the patient's body.

There are several different staging systems. Many of these have been created for specific kinds of cancers. Others can be used to describe several types of cancer.

One common system that many people are aware of puts cancer on a scale of 0 to IV.

- Stage 0 is for abnormal cells that haven't spread and are not considered cancer, though they could become cancerous in the future. This stage is also called "in-situ."
- Stage I through Stage III are for cancers that haven't spread beyond the primary tumour site or have only spread to nearby tissue. The higher the stage number, the larger the tumour and the more it has spread.
- Stage IV cancer has spread to distant areas of the body.

(University of Texas, MD Anderson Cancer Center. 2025).

Incidence of Melanoma of the Female Genitalia

The latest edition of the National Cancer Registry (2023) does not provide any information regarding melanoma of the female genitalia.

The Role of BRCA Gene Mutation

BRCA is an abbreviation originating from Br(east) Ca(ncer) and are tumour suppressor genes. Every cell in a human body contains them. There are two types: BRCA1 and BRCA2. Their main function in the body is to repair DNA, keep other genes healthy, and prevent cancerous changes. These genes can become mutated.

A mutation is a change in the gene which makes the gene stop doing its main function, therefore, no longer keeping abnormal cell growth in check. These changes (mutations) can be inherited or passed on from parents, grandparents, and great grandparents.

If someone has a gene mutation, their risk of cancer increases.

Anyone can have a BRCA gene mutation. Though, they are more commonly found in certain ethnic groups, including Ashkenazi Jews, Afrikaners, French Canadians, and people of Icelandic backgrounds. The most common cancers that can result from BRCA gene mutations are breast cancer, ovarian cancer, and prostate cancer. The full list includes.

WOMEN

BRCA1

Breast cancer
Ovarian cancer
Pancreatic cancer

BRCA2

Breast cancer
Ovarian cancer
Pancreatic cancer
Melanoma

MEN

BRCA1

Breast cancer
Prostate cancer
Pancreatic cancer

BRCA2

Breast cancer
Prostate cancer
Melanoma
Pancreatic cancer

If someone has a BRCA mutation, they may pass the mutation to their children. Each child has a 50% chance of inheriting their parents' BRCA gene mutation. One's siblings may also have inherited the BRCA gene mutation.

(National Cancer Institute, 2024; Casaubon, J.T., Kashyap, S. & Regan, J.P. 2025).

Risk Factors for Vulvo-vaginal Melanoma

Risk factors for vulvo-vaginal melanoma include:

Increased age

Smoking

Intraepithelial neoplasia of the vulva (VIN)

Human Immunodeficiency virus infection

Exposure to Human Papilloma Virus (HPV)

(Cleveland Clinic, 2023).

Signs and Symptoms of Vaginal Cancer

Women with vaginal cancer may experience the following symptoms or signs. Sometimes, women with vaginal cancer may not show any of these symptoms. Or, these symptoms may be caused by a medical condition that is not cancer.

The most common symptom of vaginal cancer may include abnormal vaginal bleeding. Vaginal bleeding, during or after menopause, is not normal and is a sign of a problem. Other symptoms of vaginal cancer may include:

- Abnormal vaginal discharge
- Difficulty or pain when urinating
- Pain during sexual intercourse
- Pain in the pelvic area (the lower part of the abdomen between the hip bones)
- Pain in the back or legs
- Swelling in the legs
- Unusual vaginal bleeding, for example, after intercourse or after menopause.
- Watery vaginal discharge.
- A lump or mass in the vagina.
- Painful urination.
- Constipation.
- Pelvic pain

If a woman is concerned about one or more of the symptoms or signs on this list, she should consult a physician. He/she will conduct a physical examination and also ask how long and how often the symptom(s) have been around, in addition to other questions.

If cancer is diagnosed, relieving symptoms remains an important part of cancer care and treatment. This may also be called symptom management, palliative care, or supportive care. Be sure to talk with the health care team about symptoms experienced, including any new symptoms or a change in symptoms.

(Healthline, 2023; Centers for Disease Control and Prevention (CDC), 2024); Moffitt Cancer Center, No date).

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Treatment of Melanoma of the Vulva and Vagina

Surgery may be the best treatment regime that could possibly significantly improve longevity of patients.

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January 2026

Treatment may include:

- Postoperative adjuvant therapy using chemotherapy
- Radiation therapy
- Topical creams immunotherapy
- Targeted therapy may help prevent recurrence of the tumour

(Cleveland Clinic, 2023; American College of Surgeons, 2022; Mayo Clinic, 2025; Bai, S., Wu, Q., Song, L. & Wu, W. 2023).

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: <https://pactr.samrc.ac.za/>

Summary for the Average Reader

Vulvo-vaginal melanoma is a rare and aggressive cancer of the female genital tract. Treatment for 2026 continues to be highly individualized and is often extrapolated from protocols used for cutaneous (skin) melanoma.

Surgical Treatment

Surgery remains the primary treatment for localized disease.

- Wide Local Excision (WLE): The standard approach for both vulvar and vaginal melanoma, aiming for clear margins (typically 1–2 cm depending on tumour thickness).
- Vulvectomy or Vaginectomy: In cases of larger or more invasive tumours, surgeons may remove part or all of the vulva or vagina.
- Sentinel Lymph Node Biopsy (SLNB): Used to check if cancer has spread to nearby lymph nodes in the groin, avoiding more radical node removal if possible.
- Pelvic Exenteration: Reserved for advanced or recurrent cases where the cancer has spread to multiple pelvic organs.

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Systemic and Targeted Therapies

These treatments are often used when the cancer has spread or cannot be fully removed by surgery.

- Immunotherapy: Immune checkpoint inhibitors like nivolumab and ipilimumab have shown significant efficacy, sometimes used in combination.
- Targeted Therapy: Doctors test for specific genetic mutations to guide treatment.
 - c-KIT Mutations: Common in mucosal melanomas; drugs like imatinib or nilotinib may be used.
 - BRAF Mutations: Less common than in skin melanoma, but if present, drugs like dabrafenib and trametinib can be effective.
- Chemotherapy: Generally considered a secondary option for mucosal melanomas, using drugs like dacarbazine or temozolomide, though response rates are often lower than with other therapies.

Radiation Therapy

Radiation is typically used as a supportive or secondary treatment.

- Adjuvant Therapy: Delivered after surgery to reduce the risk of local recurrence, particularly if lymph nodes were involved.
- Palliative Care: Used to manage symptoms like bleeding or pain in advanced stages.
- Alternative to Surgery: In patients unable to undergo surgery, techniques like stereotactic body radiotherapy (SBRT) or carbon ion radiotherapy may be considered.

Clinical Trials

Because these melanomas are rare, specialized centers strongly advocate for participation in clinical trials to access emerging therapies.

(AI Overview, 2026).

Medical Disclaimer

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