Squamous Cell Carcinoma of the Anal Canal: Disease State Overview

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Disease Epidemiology and Etiology

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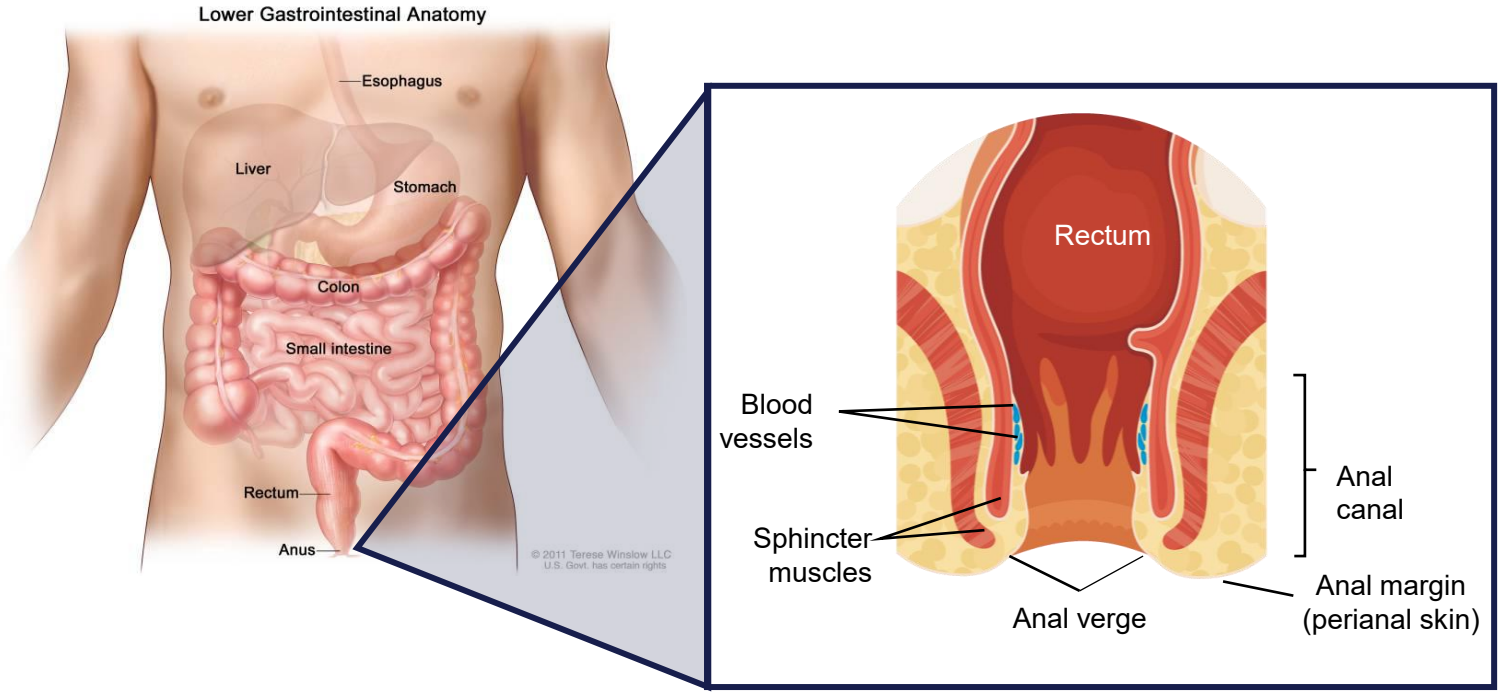
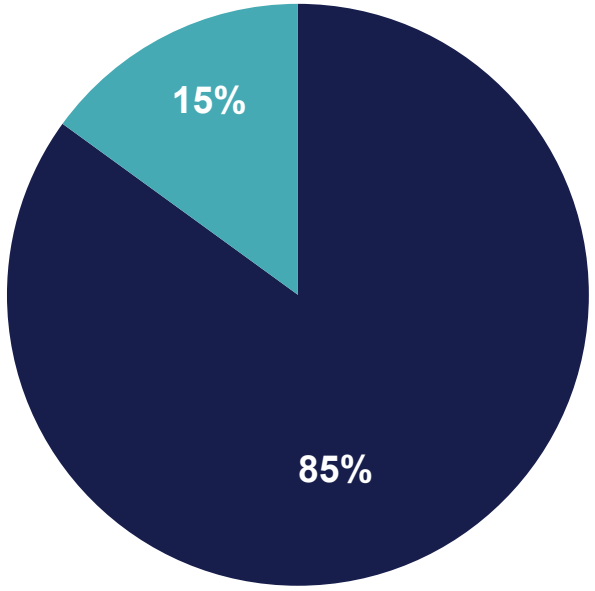
Anal Cancer is a Cancer of The Lower GI Tract



Carcinomas arise from cells that line the anal canal and margin[1-3]

Proportion of Anal Cancer Types[4]



GI, gastrointestinal; SCAC, squamous cell carcinoma of the anal canal.

1. Shridhar R, et al. *CA Cancer J Clin*. 2015;65:139–62. 2. American Cancer Society. Accessed Jan 2025. https://www.cancer.org/cancer/anal-cancer/about/what-is-anal-cancer.html. 3. National Cancer Institute. Accessed Jan 2025. https://www.cancer.gov/types/anal/patient/anal-treatment-pdq. Lower Gastrointestinal Anatomy 2022; ©2022 Terese Winslow LLC, U.S. Govt. has certain rights. 4. Symer MM, Yeo HL. F1000Research. 2018;7:F1000 Faculty Rev-1572.

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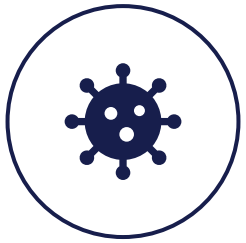
Risk Factors for Anal Cancer



HPV Infection[1,2]

- ~90% of anal cancers are associated with HPV infection
- Genotypes HPV16 and HPV18 are associated with the greatest risk and are linked to 92% of anal cancers

Immunosuppression[3,4]

- Immunosuppression is associated with increased incidence of anal cancer
- Immunosuppression can be caused by solid organ transplant, long-term steroid use for the treatment of autoimmune disease, or HIV

Other[4-6]

- Anal intercourse
- Number of sexual partners
- Smoking

HPV Infection is the Strongest Risk Factor for Anal Cancer[1]

HPV, human papilloma virus; HIV, human immunodeficiency virus.

1. Anal Cancer Foundation. Accessed Jan 2025. https://www.analcancerfoundation.org/anal-cancer/what-is-anal-cancer/hpv-cancer. 2. Silva Dalla Libera L, et al. *J Oncol*. 2019;2019:6018269. 3. Wang CJ, et al. *Surg Oncol Clin N Am.* 2017;26:17–31. 4. Shridhar R, et al. *CA Cancer J Clin*. 2015;65:139-162. 5. Krzyowska-Firych J, et al. *J Infect Public Health*.2019:12:1-6. 6. Daling J, et al. *Cancer*. 2004;101:270-280.

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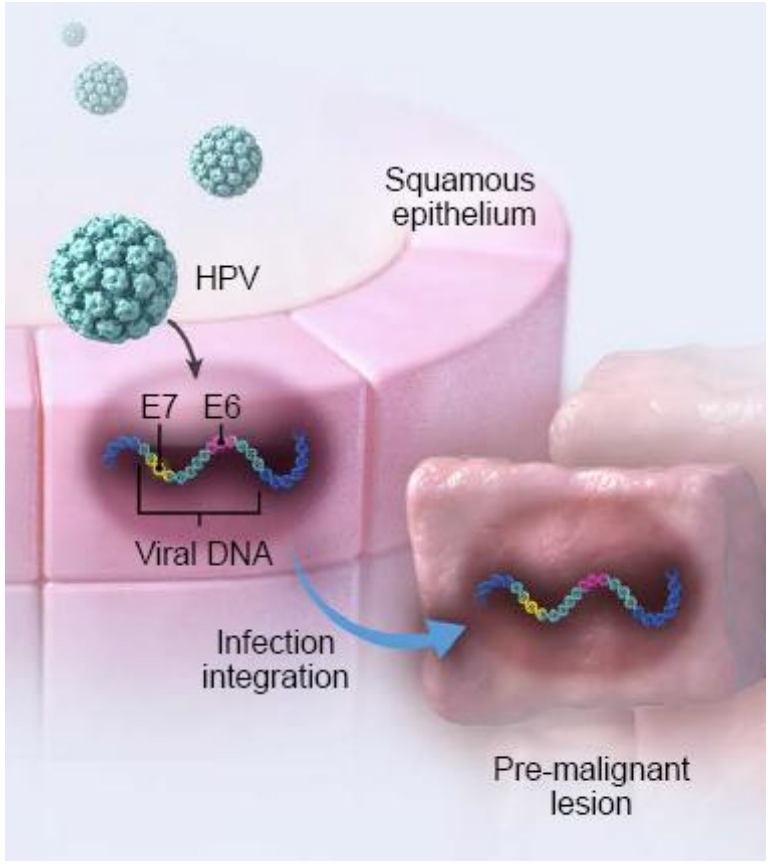
Risk Factors for Anal Cancer: HPV Infection

HPV is the common tumor-initiating event in SCAC, cervical cancer, and HNSCC



Virus targets proliferating basal cells in the squamous epithelium.

Stable integration and expression of HPV genomic elements into the host genome induces pre-malignant lesions

Pre-malignant lesions can progress to cancer

HPV Infection

HNSCC, head and neck squamous cell carcinoma.

1. Centers for Disease Control and Prevention. Accessed Jan 2025. https://www.cdc.gov/cancer/hpv/cases.html. 2. Krzowska-Firych J, et al. *J Infect Public Health*. 2019;12:1-6.

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Risk Factors for Anal Cancer: Immunosuppression

Immunosuppression plays a pivotal role in the pathogenesis of anal cancer[1-3]

- Reduces the ability to combat viral infection and control oncogenic viral processes[1]
- Immunosuppression caused by organ transplant, long-term steroid use, or AIDS significantly increases risk of anal cancer, likely due to persistent HPV infection[1,2]
- Increases rates of anal cancer recurrence[3]

HIV infection is associated with an increased risk of HPV acquisition persistence[1,4,5]

- Approximately 28% of men and 1% of women with anal cancer also have HIV infection,[1] and risk of subsequent HPV acquisition is approximately doubled in the presence of HIV infection[4]
- The immunosuppression associated with HIV infection reduces the ability to control oncogenic viral processes, such as HPV-mediated cell transformation[1]
- HIV-RNA viral load is associated with reduced HPV clearance[4,5]

1. Wang CJ, et al. *Surg Oncol Clin N Am*. 2017;26:17–31. 2. Shridhar R, et al. *CA Cancer J Clin*. 2015;65:139-162. 3. Bingmer K, et al. *Am J Surg*. 2020;219:88-92. 4. Looker KJ, et al. *J Int AIDS Soc*. 2018;21:e25110. 5. Geskus RB, et al. *AIDS*. 2016;30:37-44.

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Most Primary Cancers of the Anal Canal Are SCAC and Impact Older Individuals

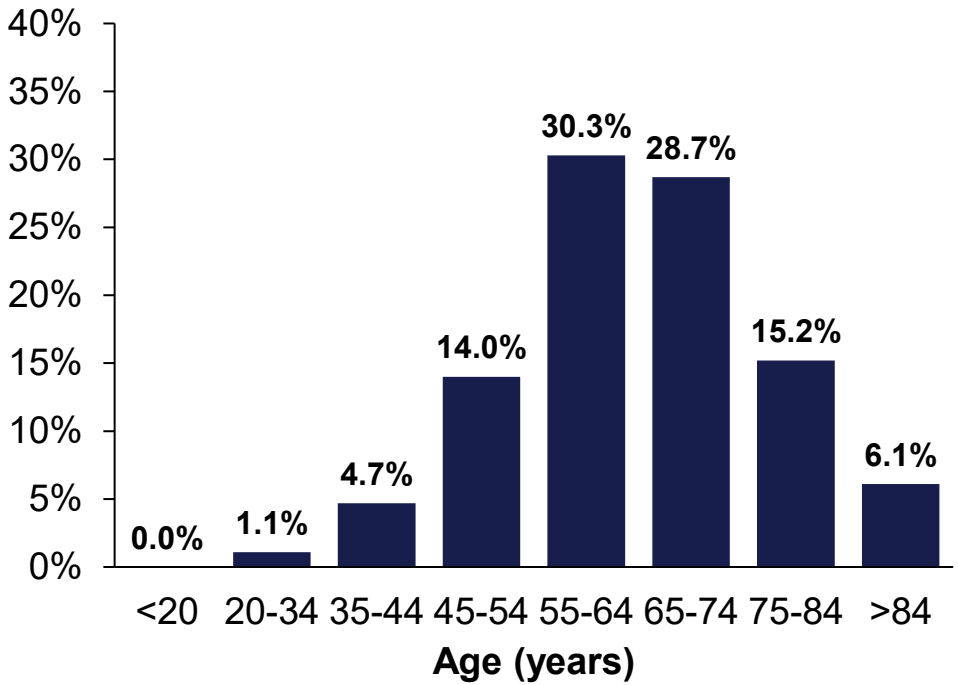
- In 2025, the estimated number of new anal cancer cases in the US was 10,930
- Annually, there are 2.0 new cases of anal cancer per 100,000 people
  - Incidence is higher in women (2.4 per 100,000) than in men (1.6 per 100,000)
- In 2022, there were an estimated 85,736 people living with anal cancer in the United States

Rates of incidence and mortality of anal cancer are rising

Incidence	Mortality
+2.2% per year[a]	**+4.1%** per year[b]

Median Age at Diagnosis **64**

Percent of New Cases by Age Group



[a] Each year over 2013-2022. [b] Each year over 2014-2022.
SCAC, squamous cell carcinoma of the anal canal.
Surveillance, Epidemiology, and End Results Program (SEER). Accessed Jan 2026. https://seer.cancer.gov/statfacts/html/anus.html. Cancer Stat Facts: Anal Cancer was originally published by the National Cancer Institute - https://seer.cancer.gov/statfacts/html/anus.html [seer.cancer.gov].

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Signs, Symptoms, and Diagnosis

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Signs and Symptoms of Anal Cancer

Important Symptoms of Anal Cancer

- Bleeding from the rectum
- Itching in or around the rectum
- A lump or mass at the anal opening
- Pain or a feeling of fullness in the anal area
- Narrowing of stool or other changes in bowel movement
- Abnormal discharge from the anus
- Incontinence of stool (loss of bowel control)
- Swollen lymph nodes in the anal or groin areas

Bleeding from the rectum is often the first sign of disease

Anal cancer can also be asymptomatic

American Cancer Society. Accessed Jan 2025. https://www.cancer.org/cancer/anal-cancer/detection-diagnosis-staging/signs-and-symptoms.html.

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Diagnosing Anal Cancer

Physical and Digital Rectal Examination[1,2]

~45% of patients with anal carcinoma present with rectal bleeding, and 30% have either pain or sensation of a rectal mass

Anoscopy[1,2]

Examination of the anus and lower rectum using a short, rigid tube called an anoscope

Endoscopy[2]

Examination of the anus and rectum using an endoscope

Chest/Abdomen CT + Pelvis CT or MRI[1,2]

Provides information on local disease extent and dissemination to other organs and is used to verify staging before treatment

FDG-PET/CT Scan[1,2]

FDG-PET/CT scan provides high sensitivity in identifying anal cancer in patients who have normal-sized lymph nodes on CT imaging

Biopsy[1,2]

Diagnosis of anal cancer is made by FNA or excisional biopsy-proven histology

Primary diagnoses are often made by gastroenterologists, colorectal surgeons, or PCPs[2]

CT, computerized tomography; FDG, fluorodeoxyglucose. FNA, fine needle aspiration; MRI, magnetic resonance imaging; PCP, primary care physician; PET, positron emission tomography.

1. Referenced with permission from the Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Anal Carcinoma V.1.2026. © National Comprehensive Cancer Network, Inc. 2026. All rights reserved. Accessed February 6, 2026. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. 2. American Cancer Society. Accessed Jan 2026. https://www.cancer.org/cancer/anal-cancer/detection-diagnosis-staging/how-diagnosed.html.

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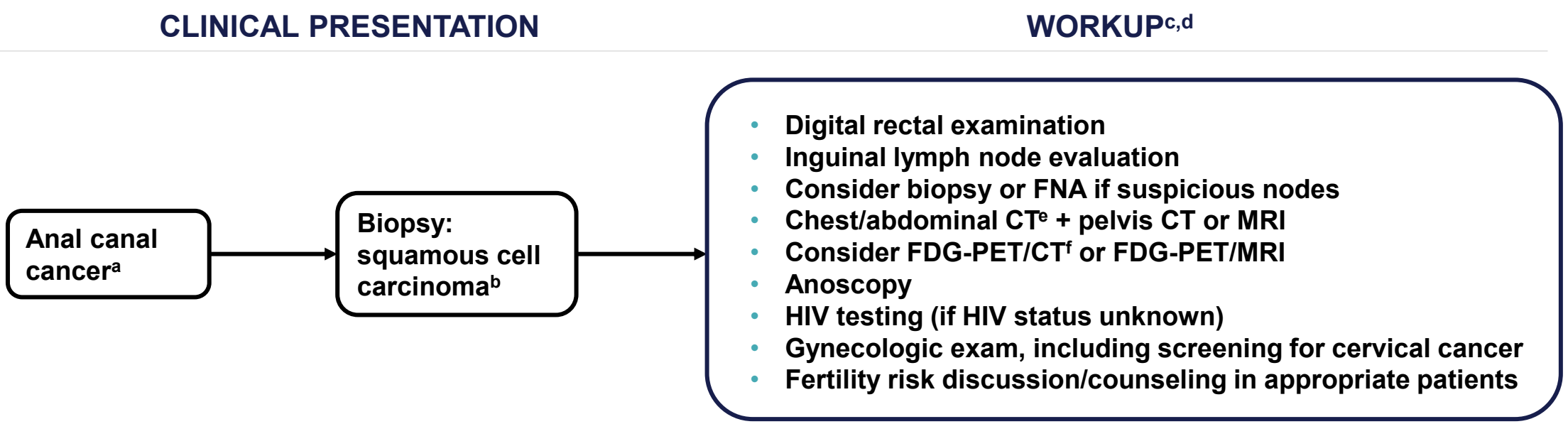
NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Anal Cancer: Diagnostic Workup



[a] The superior border of the functional anal canal, separating it from the rectum, has been defined as the palpable upper border of the anal sphincter and puborectalis muscles of the anorectal ring. It is approximately 3 to 5 cm in length, and its inferior border starts at the anal verge, the lowermost edge of the sphincter muscles, corresponding to the introitus of the anal orifice. [b] For melanoma histology, see the NCCN Guidelines for Melanoma: Cutaneous; for adenocarcinoma, see the NCCN Guidelines for Rectal Cancer. [c] FDA added a Boxed warning to the capecitabine label, recommending to test patients for genetic variants of *DPYD* prior to initiating capecitabine unless immediate treatment is necessary. For information on *DPYD* testing and fluoropyrimidine-associated toxicity, see the NCCN Guidelines for Colon Cancer. [d] Refer to the NCCN Distress Thermometer and Problem List, which includes social determinants of health. See NCCN Guidelines for Distress Management (DIS-A). [e] CT should be with IV and oral contrast. Pelvic MRI with contrast. If IV iodinated contrast material is contraindicated due to significant contrast allergy or renal failure, then MRI examination of the abdomen and pelvis with IV gadolinium-based contrast agent can be obtained in select patients (see American College of Radiology contrast manual: https://www.acr.org/-/media/ACR/Files/Clinical-Resources/Contrast_Media.pdf). IV contrast is not required for the chest CT. [f] FDG-PET/CT scan does not replace a diagnostic CT. PET/CT performed skull base to mid-thigh.
IV, intravenous.

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Staging and Prognosis

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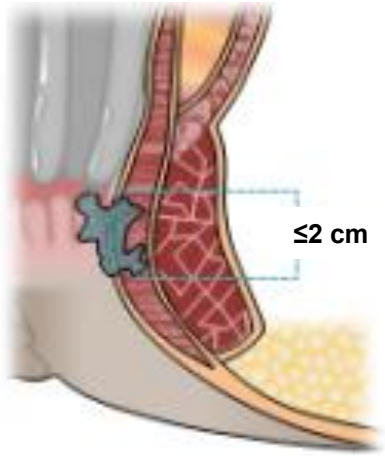
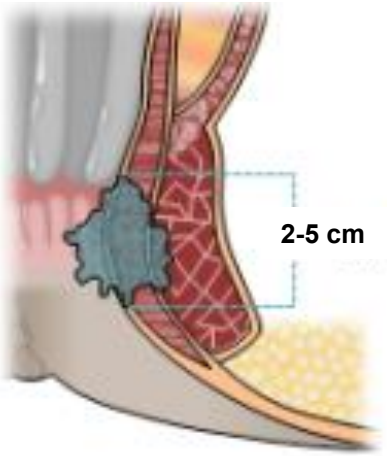
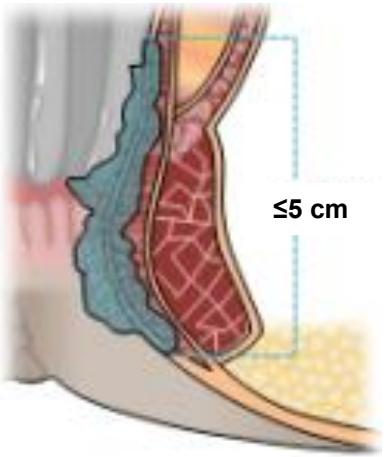
Anal Cancer Staging

AJCC TNM Staging Classification for Anal Carcinoma

Stage	I	IIa	IIb
Description			
Primary tumor (T)	T1 (≤2 cm)	T2 (2–5 cm)	T1-T2 (≤5 cm)
Regional lymph node (N)	N0	N0	N1
Distant metastasis (M)	M0	M0	M0

AJCC, American Joint Committee on Cancer; M0, no distant metastasis; N0, no regional lymph node metastasis; N1, metastasis to lymph nodes near the rectum; TMN, tumor, node, metastasis.

American Cancer Society. Accessed Jan 2025. https://www.cancer.org/cancer/types/anal-cancer/detection-diagnosis-staging/staging.html.

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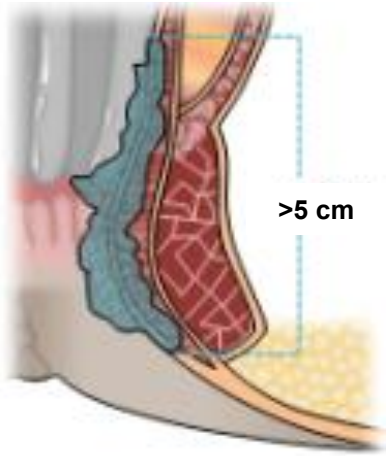
Anal Cancer Staging (cont)

AJCC TNM Staging Classification for Anal Carcinoma

Stage	IIIa	IIIb	IIIc	IV
Description		Any size, invading adjacent organs	Any size, invading adjacent organs	Any tumor with distant metastasis
Primary tumor (T)	T3 (>5 cm)	T4	T4	Any T
Regional lymph node (N)	N0 or N1	N0	N1	Any N
Distant metastasis (M)	M0	M0	M0	M1

N1, nearby lymph nodes; M1, distant metastasis.

American Cancer Society. Accessed Jan 2026. https://www.cancer.org/cancer/types/anal-cancer/detection-diagnosis-staging/staging.html.

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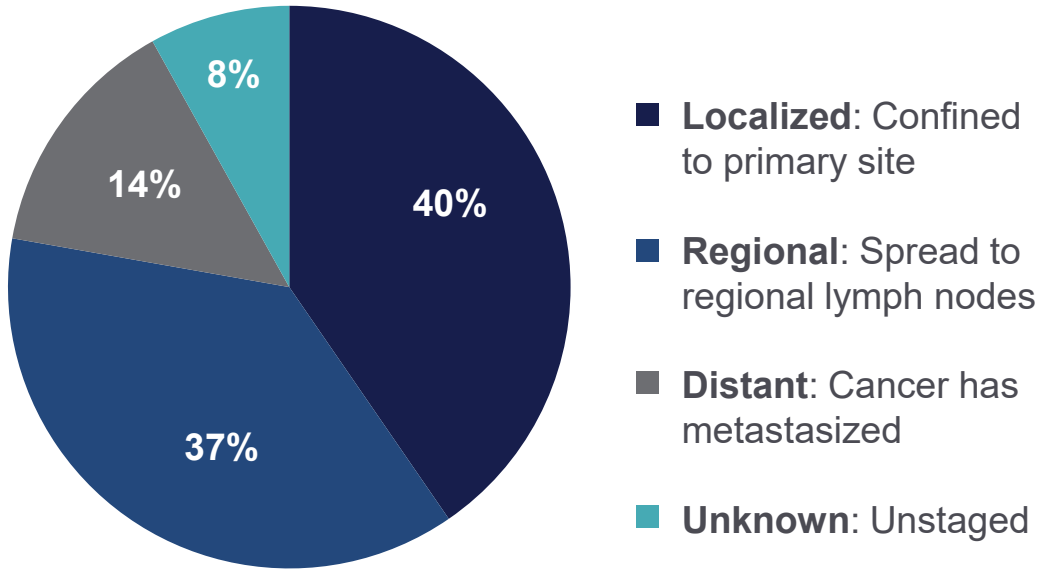
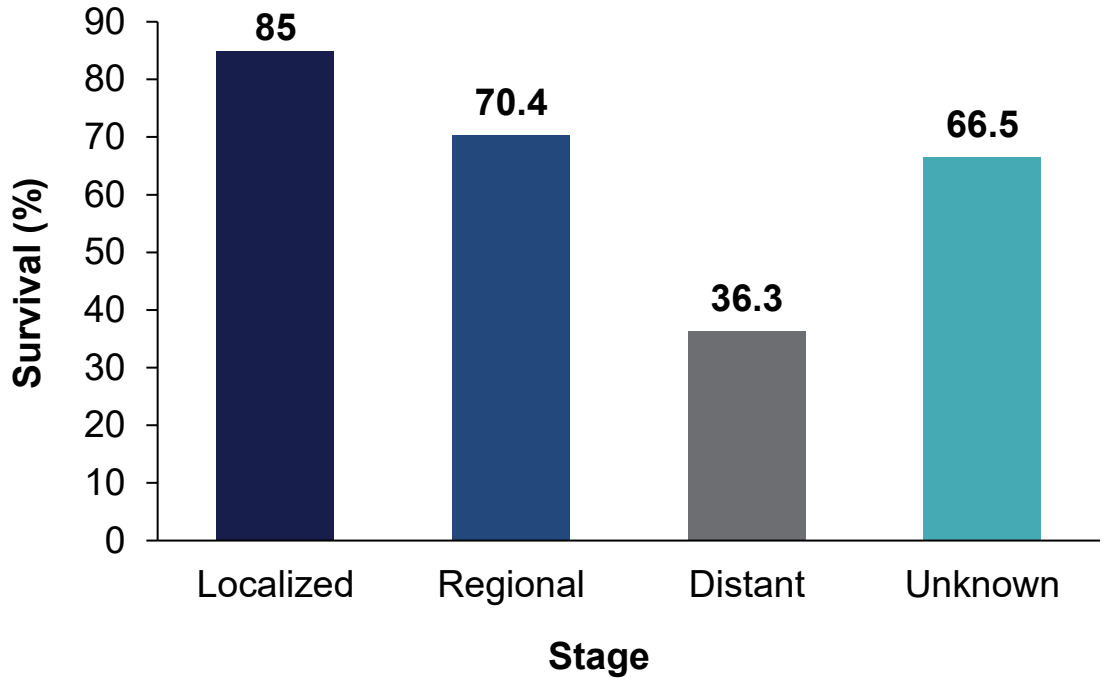
Anal Cancer Stage at Diagnosis and Survival Rates

Percent of Cases by Stage at Diagnosis (USA)[a,b]



5-year Survival by Stage at Diagnosis (USA)[a]



[a] SEER 22 (Excluding IL, MA) 2014–2020, all races, both sexes by SEER Summary Stage. [b] Data have been rounded to the nearest whole number. Surveillance, Epidemiology, and End Results Program (SEER). Accessed Jan 2026. https://seer.cancer.gov/statfacts/html/anus.html. Cancer Stat Facts: Anal Cancer was originally published by the National Cancer Institute - https://seer.cancer.gov/statfacts/html/anus.html [seer.cancer.gov].

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