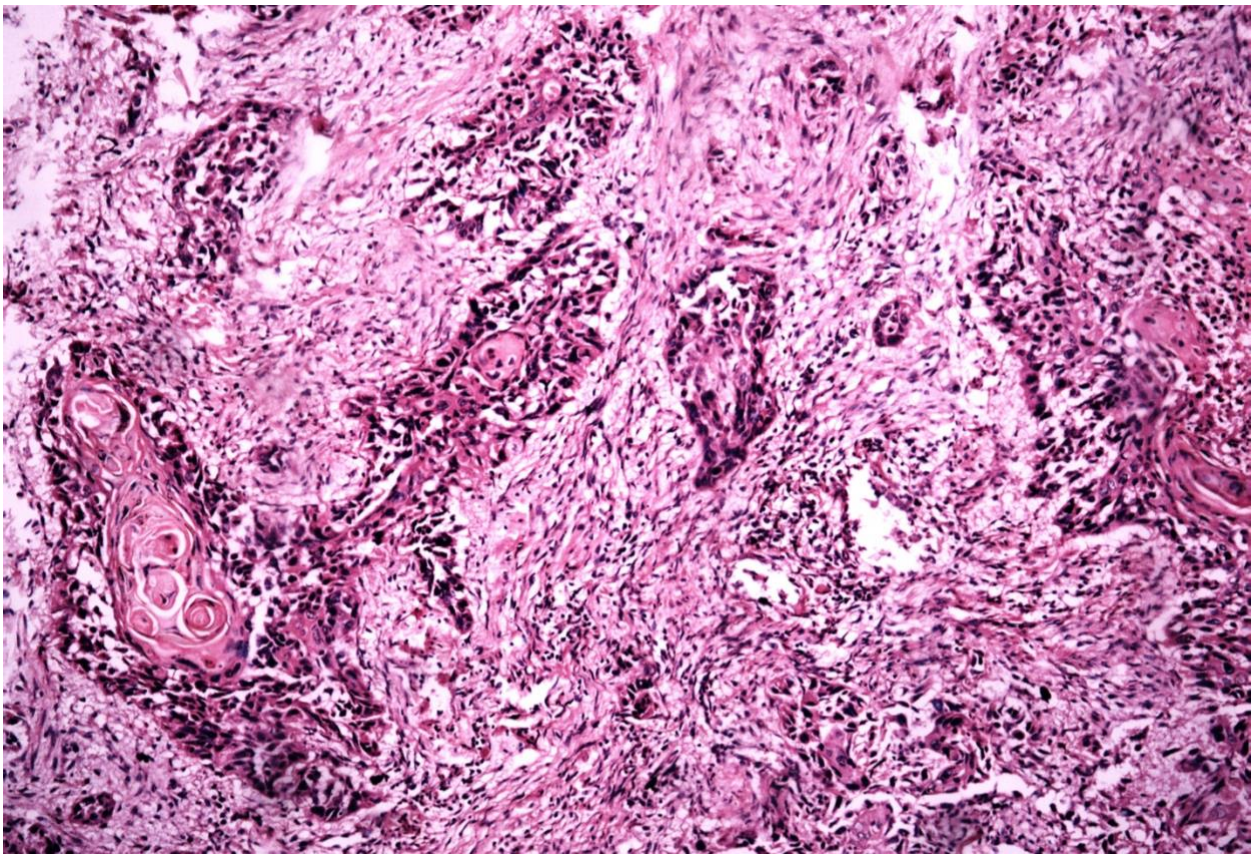

Standard of Care:
Comprehensive Guide to Cancer Screening

A Focus on Oral and Lip, Esophageal, Gastric, Colo-Rectal, Anal, Cervical, Breast, Skin and Lung Cancer

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THE CENTER FOR INNOVATION AND TRANSLATION OF POC TECHNOLOGIES FOR EQUITABLE CANCER CARE

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Introduction

Welcome to the **Center for Innovation and Translation of POC Technologies for Equitable Cancer Care (CITEC)** Program Standards of Care Document. This guide is a collaborative effort involving engineers, oncologists, and global health partners dedicated to advancing cancer care by developing and implementing point-of-care (POC) technologies.

About CITEC

CITEC stands as a testament to the power of collaboration, uniting a global community of investigators with the shared mission of developing affordable and effective POC technologies for early cancer detection. By bringing together experts from diverse fields, CITEC aims to identify, accelerate the development of, evaluate, and implement POC technologies that address the critical need for improved cancer detection on a global scale.

Our Mission

At the heart of CITEC's mission lies a commitment to developing technologies that transcend geographical and economic barriers, ensuring equitable access to early cancer detection. Our focus is not only on advancing technology but also on training local users and technology developers to create and disseminate these vital POC technologies, thereby contributing to a more inclusive and accessible global healthcare landscape.

Standards of Care Document

This document serves as a comprehensive guide to the Standards of Care within the CITEC Program. Specifically tailored for researchers in the field of biomedical engineering, cancer prevention, and early detection, as well as Global Medical Innovation (GMI) students at Rice University, this guide is designed to facilitate the assessment of needs in cancer care.

How to Use This Document

For researchers and students engaging in 'needs finding' activities locally and globally, this document outlines the Standards of Care for various cancers. It provides insights into screening and diagnostic procedures, point-of-care pathologies, WHO recommendations, considerations for high and low-resource settings, guidelines, and emerging technologies and clinical trials. Each section is crafted to inform and guide the work of those dedicated to advancing cancer care.

As we collectively work towards a future where early cancer detection is accessible to all, this document serves as a foundational resource, aligning our efforts and inspiring innovation. Thank you for being a part of the CITEC community and contributing to the transformation of cancer care on a global scale. Together, we can make a difference.

Oral and Lip Cancer

Statistics And Risk Factors
• 16th place in incidence and mortality worldwide in 2020 [LO1] • 377,000 new cases and 177,000 deaths in 2020. 5-year survival: 68-90% [LO11] • 2/3 of lesions are identified at an advanced stage [LO12] • Risk Factors: tobacco use, heavy alcohol use, and human papillomavirus (HPV16) infection and EBV infection [LO4,10]

Screening

Guidelines
A thorough oral, head, and neck exam, conduct a history with risk assessment of patients regularly, and perform a visual and tactile exam of the head neck, and oral cavity in patients identified as having risk factors and/or signs and symptoms. The exam requires adequate lighting, a dental mouth mirror or tongue depressor, 2 x 2 gauze, and gloves. With the patient seated, the extraoral and perioral tissues are examined first, followed by the intraoral tissues. The head/scalp, face, ears, and neck are inspected. The regional lymph node areas of the head. [LO2,4,5]
WHO Recommendations Standard Clinical Oral Examination: white-light visual examination and palpation of the oral cavity structures and the external facial and neck regions. *There is no universally recognized, evidence-based determination of what constitutes an appropriate oral cancer screening examination.

Standard of Care	
Visual Oral Examination/Clinical Oral Examination	
If lesions are seen in the mouth Toluidine Blue Stain: Toluidine blue stain is used in oral cancer screenings to highlight areas with increased cellular activity or abnormalities, aiding in the identification of potentially cancerous lesions during examinations. [LO2]	**Fluorescence Staining** Fluorescence staining involves the application of fluorescent dyes to oral tissues, enhancing visualization of cellular changes and potentially identifying early signs of oral cancer through fluorescence-based diagnostic methods. [LO2]
Exfoliative Cytology Exfoliative cytology in oral cancer screenings involves collecting cells from the oral mucosa, allowing for microscopic examination to detect abnormal cellular changes, aiding in the early diagnosis of oral lesions. [LO2,3]	**Brush Biopsy** A brush biopsy is a non-invasive method that utilizes a specialized brush to collect cells from suspicious oral lesions, providing a tool for obtaining diagnostic samples and aiding in the identification of potential malignancies in oral tissues. [LO2,3]

Emerging Technologies and Clinical Trials	
Wide-field and High-Resolution In Vivo Imaging in Visualizing Lesions in patients with Oral Neoplasia Undergoing Surgery using a widefield multispectral imaging device and a high-resolution optical system (high-resolution microendoscope HRME) [OC14]	**Multimodal optical imaging with real-time projection of cancer risk and biopsy guidance maps for early oral cancer diagnosis and treatment:** portable active biopsy guidance system (ABGS) that uses multimodal optical imaging with deep learning to directly project cancer risk and biopsy guidance maps onto oral mucosa in real-time. [OC 13]

Country-Specific Examples (Screening, Diagnostics, Early Treatment)	
Costa Rica Oral Cancer screening is not currently conducted in Costa Rica.	**Brazil** Hospital de Amor has a screening program that implies Visual Oral Examination/ Clinical Oral Examination and Biopsy of suspicious lesions

United States	**Mozambique**
Country-Specific Unmet Needs (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil** POC tool that can better visualize early Oral Cancer than visual inspection to improve early detection rates. There is a need to be able to track the progression of pre-cancerous lesions in the lower lip to improve outcomes for those patients
United States	**Mozambique**
Country-Specific Preferences for POC Screening	
Costa Rica	**Brazil**
United States	**Mozambique**

ORAL AND LIP CANCER

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Esophageal Cancer

Statistics And Risk Factors
• 8th most diagnosed and the 6th most common cause of cancer death in the world [E5] • 604,000 new cases and 544,000 deaths in 2020 • Risk Factors: Tobacco, alcohol use, high BMI [EC 4]

Screening

Guidelines [E1]
• Screening with standard upper endoscopy may be considered in individuals with at least 3 established risk factors for Barrett's esophagus (BE) and esophageal adenocarcinoma, including individuals who are male, non-Hispanic white, age >50 years, have a history of smoking, chronic gastroesophageal reflux disease, obesity, or a family history of BE or esophageal adenocarcinoma. For squamous cell cancer, screening with upper endoscopy can be considered as well for patients with known or prior head and neck cancer (or in high-risk 'regions' such as northern China, etc.) • Non-endoscopic cell-collection devices (e.g. Cytosponge) may be considered an option to screen for BE. • Screening and surveillance endoscopic examination should be performed using high-definition white light endoscopy and virtual chromoendoscopy, with endoscopists spending adequate time inspecting the Barrett's segment. • Endoscopy- not standard or routine screening, just diagnostic for symptomatic or at-risk patients.
WHO Recommendations Screening: when abnormalities are identified during screening, further tests to establish a definitive diagnosis should follow, as should referral for treatment if cancer is proven to be present.

Diagnostic Procedures

Standard of Care
Endoscopy Endoscopy involves the use of a flexible tube with a light and camera to visually examine internal organs, facilitating precise diagnostics and exploration of abnormalities in various areas of the body.

Emerging Technologies and Clinical Trials	
Saliva or Stool POC (Pre-endoscopy) Saliva or stool point-of-care (POC) testing, conducted before endoscopy, offers a non-invasive approach to screen for specific biomarkers, providing valuable insights into gastrointestinal health and aiding in risk assessment.	**Unsedated Trans nasal Endoscopy** Unsedated trans-nasal endoscopy is a minimally invasive procedure that utilizes a thin, flexible tube inserted through the nose to examine the upper gastrointestinal tract, offering a comfortable alternative for diagnostic evaluations.
Esophageal Capsule Endoscopy (ECE) Esophageal capsule endoscopy involves a small, swallowable capsule equipped with a camera to capture images of the esophagus, providing a less invasive alternative for diagnostic examinations and early detection of esophageal conditions.	**SOS (Sponge on a String Cell Sampling Device - Mayo Clinic)** The SOS device, or sponge on a string, developed by the Mayo Clinic, allows for convenient and targeted cell sampling in the gastrointestinal tract, facilitating diagnostic procedures and contributing to the early detection of abnormalities.
EsophaCap for Early Detection of Early Esophageal Carcinoma EsophaCap, designed for early detection of esophageal carcinoma, employs advanced technology to capture cellular changes, aiding in the early diagnosis of esophageal cancer and facilitating timely intervention. [E2]	**Oral Microbiome for Barrett's Esophagus** Analyzing the oral microbiome provides insights into the microbial community in the mouth, offering a potential biomarker for the presence of Barrett's esophagus and contributing to non-invasive diagnostic approaches for this condition. [E3]
Balloon Cytology Balloon cytology employs an inflatable device to collect cells from targeted areas, providing a minimally invasive method	**Sponge Cytology** Sponge cytology utilizes a sponge-like device to collect cellular samples, offering a gentle yet effective approach to

for diagnosing cellular abnormalities and assisting in the detection of early signs of cancer.	diagnose abnormalities in specific tissues, contributing to accurate and early cancer detection.
NGS of a Multigene Panel in cfDNA from Plasma Samples Next-Generation Sequencing (NGS) of a multigene panel in circulating free DNA (cfDNA) from plasma samples enables a comprehensive analysis of genetic alterations, aiding in the diagnosis of cancer and providing valuable information for personalized treatment strategies.	

High vs. Low Resource Settings	
High Resource Screenings for Barret's esophagus have been used in clinics individually in high-income countries, but no randomized controlled trials have shown a significant benefit. Population-based endoscopic screening will require well-trained health workers with diverse skills as well as considerable infrastructure; these are not widely available, especially in low- and middle-income countries, where most cases of esophageal squamous cell carcinoma occur	**Low Resource**
Country-Specific Examples (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil**
United States	**Mozambique**
Country-Specific Unmet Needs (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil** There is a need for a non-endoscopic method to screen for esophageal cancer that improves cost-effectiveness in screening.
United States	**Mozambique**
Country-Specific Preferences for POC Screening	
Costa Rica	**Brazil** Ease of use, Sensitivity, Specificity, and cost were rated as extremely important for a POC tool.
United States	**Mozambique**

ESOPHAGEAL CANCER

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Gastric Cancer

Statistics And Risk Factors
• 5th most common worldwide [GC9], 4th leading cause of cancer death worldwide [GC9] • 36% - 5-year survival rate [GC10] • Cardia: Obesity and reflux, non-Cardia: H. pylori (90%). [GC 10] • Other Factors: cigarette smoking, diets high in salt and processed meats [GC 8]

Screening

Guidelines
None are provided
WHO Recommendations: None are provided

Diagnostic Procedures

Standard of Care
Endoscopy Endoscopy involves using a flexible tube with a light and camera to visually examine internal organs, facilitating precise diagnostics and exploration of abnormalities in various areas of the body.

Emerging Technologies and Clinical Trials	
Breath Biomarkers Emerging technologies in stomach cancer care involve the detection of breath biomarkers, offering a non-invasive method to identify specific compounds indicative of gastric abnormalities, aiding in early diagnosis and monitoring treatment response. [GC2,3,6]	**ABC Method** Serum H. pylori and Pepsinogen: The ABC method, utilizing serum levels of H. pylori and pepsinogen, represents an innovative approach for risk assessment and early detection of stomach cancer, providing a standardized method to evaluate biomarkers associated with gastric health. [GC2,4]
Exhale Breath Samples Collection and analysis of exhaled breath samples present a novel avenue for stomach cancer diagnostics, enabling the identification of volatile organic compounds that may serve as indicative biomarkers for early detection and monitoring. [GC2,3,6]	**Use of Blood Biomarkers to Predict Gastric Cancer Risk** The utilization of blood biomarkers for predicting gastric cancer risk represents a promising advancement in personalized medicine, offering a non-invasive means to assess individual susceptibility and facilitate targeted preventive strategies.[GC2]
Confocal Endoscopic Microscopy Confocal endoscopic microscopy is an advanced imaging technology that allows real-time visualization of cellular structures during endoscopy, contributing to enhanced diagnostic precision and guiding targeted interventions for stomach cancer care when used with NBI or chromoendoscopy [GC7]	**Rapid serological test for gastric cancer screening (CITEC project)** Rapid blood test for multiplexed detection of three serological biomarkers (pepsinogen I [PG1], pepsinogen II [PG2] and H. pylori antibodies)

High vs. Low Resource Settings	
High Resource	**Low Resource**

Country-Specific Examples (Screening, Diagnostics, Early Treatment)	
Costa Rica Costa Rica's Gastric and Colorectal Cancer screening program (Japanese cooperation) targets high-incidence areas.	**Brazil** No national guidelines for screening

An early detection center in Cartago screens 40 patients daily using fluoroscopy, referring suspicious cases for endoscopy. A bus is sent to pick up the patients and bring them to the center.	
United States	**Mozambique**
Country-Specific Unmet Needs (Screening, Diagnostics, Early Treatment)	
Costa Rica There is a need for a less resource-intensive method to screen for gastric cancer that is more cost-effective and easy to deploy than photofluorography or upper endoscopy.	**Brazil** There is a need for a less resource-intensive method to screen for gastric cancer that is more cost-effective and easy to deploy than photofluorography or upper endoscopy.
United States	**Mozambique**
Country-Specific Preferences for POC screening	
Costa Rica	**Brazil** Ease of use, Sensitivity, Specificity and cost were rated as extremely important for a POC tool
United States	**Mozambique**

GASTRIC CANCER

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Colorectal Cancer

Statistics And Risk Factors [CRC 1]
• 3rd most common worldwide • 1.9 Million new cases and 900 K deaths in 2022 • 5 year survival rate 10-90% depending on the extent of the disease. • Risk factors: Diet, obesity, smoking, alcohol

Screening

Guidelines	WHO Guidelines		
The American Cancer Society 2018 guideline for colorectal cancer screening recommends that average-risk adults aged 45 years and older undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) exam, based on personal preferences and test availability. As a part of the screening process, all positive results on non-colonoscopy screening tests should be followed up with timely colonoscopy. [CRC3, 4,5]	**Screening Method**	**Interval Age**	**Range**
	Interval Age Guaiac Fecal Occult Blood Test (gFOBT)	2 years	45-50 to 75 years
	Higher-Sensitivity Guaiac Fecal Occult Blood Test (gFOBT) (with Rehydration)	1 or 2 years	45-50 to 75 years
	Fecal Immunochemical Test for Hemoglobin (FIT)	2 years	45-50 to 75 years
	Sigmoidoscopy	Every 5 years	45-50 to age 75
	Colonoscopy	Every 10 years	45-50 to age 75
	Computed Tomography (CT) Colonography	Every 5 years	45-50 to age 75

Diagnostic Procedures

Standard of Care Colorectal Cancer Screening	
Guaiac Fecal Occult Blood Test (gFOBT) The guaiac fecal occult blood test detects hidden blood in stool, serving as an initial screening method for colorectal cancer, aiming to identify potential abnormalities that may warrant further investigation. [CRC2,4]	**Higher-Sensitivity Gualac Fecal Occult Blood Test (gFOBT) (with Rehydration)** The higher sensitivity gFOBT, incorporating rehydration, enhances the detection of occult blood in stool, providing an improved screening tool for colorectal cancer to increase sensitivity and reduce false-negative results. [CSC2,5]
Fecal Immunochemical Test for Hemoglobin (FIT) The fecal immunochemical test (FIT) detects the presence of hemoglobin in stool, offering a more specific and sensitive approach to colorectal cancer screening, with the potential to identify early signs of the disease. [CRC2,5]	**Sigmoidoscopy** Sigmoidoscopy involves the examination of the lower part of the colon using a flexible tube, enabling direct visualization of the colorectal region and allowing for the detection of abnormalities as part of a comprehensive screening strategy. [CRC3,4]
Colonoscopy Colonoscopy is a comprehensive diagnostic procedure that involves the examination of the entire colon using a flexible tube with a camera, providing a detailed assessment of the colorectal region and allowing for the removal of precancerous polyps. [CRC3,4]	**Computed Tomography (CT) Colonography** CT colonography, or virtual colonoscopy, employs advanced imaging technology to create detailed, three-dimensional images of the colon, offering a non-invasive option for colorectal cancer screening, particularly for those who may be averse to traditional colonoscopy. [CRC3,4]
Emerging Technologies and Clinical Trials	

Novel Colon Cancer Markers in Gastrointestinal Tissue and Biofluids Exploration of novel colon cancer markers in gastrointestinal tissue and biofluids involve identifying and studying unique biomarkers present in both tissues and bodily fluids, contributing to advanced diagnostic methods and a deeper understanding of colorectal cancer. [CR6]	**HRME (High-Resolution Micro endoscopy)** High-resolution microendoscopy (HRME) utilizes advanced imaging technology for real-time, detailed visualization of cellular structures during endoscopy, offering enhanced diagnostic precision and insights into colorectal abnormalities, aiding in the early detection of colon cancer when used during colonoscopy WITH white light or NBI, as a confirmatory technique for 'resect and discard' polyps. [CR7]
High vs. Low Resource Settings	
High Resource	**Low Resource**
Country-Specific Examples (Screening, Diagnostics, Early Treatment)	
Costa Rica There is a need for a screening method better than FIT for colorectal cancer that is more cost-effective and easy to implement broadly. There is a need to increase the sensitivity/specificity of colorectal cancer screening by FIT test to reduce the resource burden of unnecessary colonoscopies.	**Brazil** There is a need for a screening method better than FIT for colorectal cancer that is more cost-effective and easy to implement broadly. There is a need to increase the sensitivity/specificity of colorectal cancer screening by FIT test to reduce the resource burden of unnecessary colonoscopies.
United States	**Mozambique**
Country-Specific Unmet Needs (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil** No national guidelines for screening
United States	**Mozambique**
Country-Specific Preferences for POC screening	
Costa Rica	**Brazil** Need for a way to determine which patients actually need a colonoscopy. Ease of use, cost and sensitivity were the highest rated requirements for POC technologies in Barretos Cancer Hospital Ease of use, Sensitivity, Specificity, and cost were rated as extremely important for a POC tool at USP
United States	**Mozambique**

COLORECTAL CANCER

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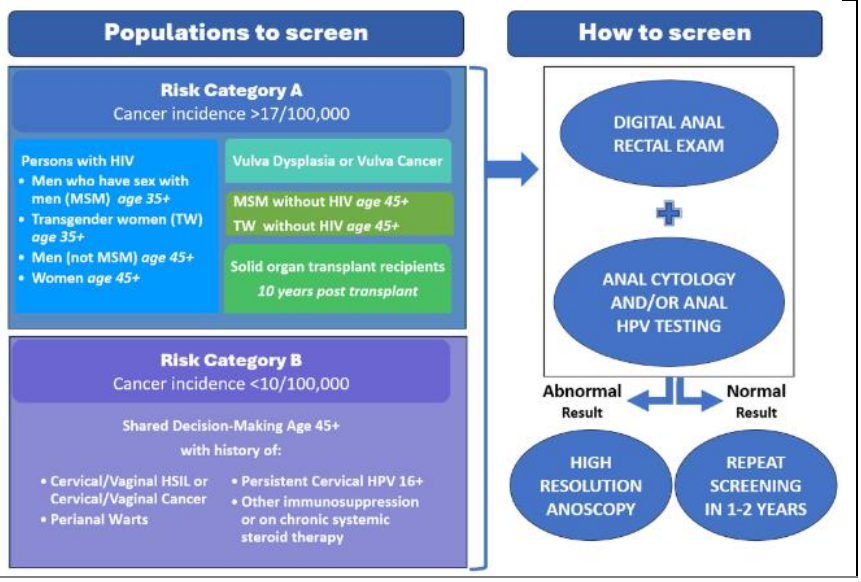
Anal Cancer

Statistics And Risk Factors [AC1,2]
• 500,000 new cases, 19000 deaths in 2020. • The major risk factor is HPV, followed by HIV. • More common in women than men. • Squamous Cell Carcinoma is the most common.

Screening

Guidelines	IANS Guidelines [AC2]
The International Anal Neoplasia Society (IANS) developed consensus guidelines for anal cancer screening among high-risk groups. There are no WHO guidelines for Anal cancer screening [AC 2,3]	

Diagnostic Procedures

Standard of Care	
Screening: Digital anorectal exam and anal swab. If the test is positive for potential signs of anal HSIL, a high-resolution anoscopy (HRA) is recommended and a biopsy will be taken [AC2,3]	HIV Clinical Guidelines Now Recommend High Resolution Anoscopy as Part of Anal Cancer Screening Program for People with HIV. If HRA is not available, the panel recommends that people with HIV continue to be screened using assessment of symptoms and DARE. People with any symptoms or who show signs of anal cancer should undergo standard anoscopy, without the collection of anal specimens for diagnosis. [AC2,3]
Emerging Technologies and Clinical Trials	
ANCHOR study: **A**nal **C**ancer **H**igh-Grade Epithelial Lesions **O**utcomes **R**esearch: NIH funded confirmed that the detection and treatment of HSIL in people with HIV is effective for anal cancer prevention. [AC2,3]	**HPV Assay on Anal Specimens** [AC 4]
High vs. Low Resource Settings	
High Resource	**Low Resource**

Country-Specific Examples (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil** No generalized screening program in Brazil
United States	**Mozambique**
Country-Specific Unmet Needs (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil**
United States	**Mozambique**
Country-Specific Preferences for POC screening	
Costa Rica	Brazil Sensitivity, Specificity, Cost, Patient comfort and patient collected were rated as highest important requirements for a POC technology in Barretos Cancer Hospital Ease of use, Sensitivity, Specificity and cost were rated as extremely important for a POC tool at USP. Painless colonoscopy with bowel prep that could see everything and treat cancer directly: virtual colonoscopy. Tool to triage, diagnose and treat.
United States	**Mozambique**

ANAL CANCER

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Cervical Cancer

Statistics And Risk Factors [CC8]
• Globally it is the 4th most common cancer in women. • 660,000 new cases and 350,000 deaths in 2022 • The major risk factors is HPV infection.

Screening

Guidelines [CC1]	Population	Recommendation
USPSTF cervical cancer screening recommendations Adopted by the American College of Obstetricians and Gynecologists (ACOG) the Society of Clinical Oncology (SGO) and the American Society for Colposcopy and Cervical Pathology (ASCCP). These recommendations apply to individuals with a cervix who do not have any signs or symptoms of cervical cancer, regardless of their sexual history or HPV vaccination status, to individuals who are at high risk of the disease, such as those who have previously received a diagnosis of a high-grade precancerous cervical lesion, and to individuals with in utero exposure to diethylstilbestrol or those who have a compromised immune system (e.g., individuals with human immunodeficiency virus). [CC1]	**< 21 years**	No screening
	21-29 years	Cytology alone every 3 years
	30-65 years	Any one of the following: • Cytology alone every 3 years • FDA-approved primary hrHPV testing alone every 5 years • hrHPV testing and cytology every 5 years
	> 65 years	No screening after adequate negative prior screening results
	Hysterectomy	No screening in individuals who do not have a history of high-grade cervical precancerous lesions or cervical cancer
WHO Recommendations for Screening **HPV testing**: minimum 2 lifetime screenings, every 5-10 years starting at age 30. **Women with HIV:** screening every 3 years starting at age 25 [CC8]		

Diagnostic Procedures

Standard of Care	
Pap Testing Pap testing, or Papanicolaou smear, involves collecting cells from the cervix to detect abnormalities or precancerous changes, aiding in the early diagnosis of cervical cancer. [CC1,2,8]	**Co-testing Pap+HPV** Co-testing combines Pap testing and HPV testing to enhance the sensitivity of cervical cancer screening, providing a comprehensive assessment of both cellular abnormalities and viral presence.[CC2]
HPV Testing and Genotypes- PRC HPV testing with Polymerase Chain Reaction (PRC) identifies the presence of high-risk human papillomavirus and determines specific genotypes, crucial for assessing the risk of cervical cancer development. [CC8}	**VIA with Acetic Acid or Lugol** Visual Inspection with Acetic Acid (VIA) or Lugol's solution involves applying substances to the cervix to visually identify abnormal areas, offering an older yet cost-effective method for cervical cancer screening. [CC8]
Emerging Technologies and Clinical Trials	
HPV Self-Testing HPV self-testing enables individuals to collect samples independently for human papillomavirus detection, providing a convenient and accessible method for early screening. [CC3]	**DNA Methylation Testing** DNA methylation testing assesses epigenetic changes, offering insights into potential cancerous alterations and contributing to the development of advanced diagnostic strategies for early cancer detection. [CC4]

HPV DNA and mRNA via Self-Collected Menstrual Blood Self-collection of menstrual blood allows for the simultaneous detection of HPV DNA and mRNA, providing a non-invasive and women-friendly approach to screening for human papillomavirus and its associated gene expression. [CC3]	**mHRME (Multi-spectral High-Resolution Micro endoscopy)** mHRME, or multi-spectral high-resolution micro endoscopy, utilizes advanced imaging technology to visualize cellular changes in real-time, aiding in the early identification of abnormalities during cervical cancer screening. [CC6]
Hand-held cervical photoacoustic and ultrasonic endoscope (cPAUSE) for diagnosis of cervical cancer (CITEC Project)	
High vs. Low Resource Settings	
High Resource	**Low Resource**
Country-Specific Examples (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil**
United States	**Mozambique**
Country-Specific Unmet Needs (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil**
United States	**Mozambique** An affordable POC tool or method to detect high risk HPV types in women in order to facilitate timely follow-up and treatment. A POC a tool to diagnose, stage, and risk-stratify prostate and cervical cancer and distinguish precancerous vs cancerous forms of the disease in a timely manner in order to facilitate appropriate treatment pathways
Country-Specific Preferences for POC screening	
Costa Rica	Brazil Ease of use, Specificity, Cost, and Sensitivity are rated as highest important requirements for a POC technology in Barretos Cancer Hospital Another provider thought all of the following aspects are extremely important for a POC tool for cervical cancer screening: Ease of use, sensitivity, specificity, cost, time to result, ability to be done without lab infrastructure, patient comfort, and self-collection. In addition, an easy method to receive the results of the test was mentioned as important.
United States	**Mozambique**

CERVICAL CANCER

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Breast Cancer

Statistics And Risk Factors [BC 4]
• Second most common cancer worldwide. • 2.3 Million new cases in women and 607,000 deaths in 2022 • 5-year survival: 10-90% depending on the stage of diagnosis and on high vs low-resource settings

Screening

Guidelines	Population	Recommendation
USPSTF: biennial screening mammography in women aged 40 to 74 years has a moderate net benefit. The USPSTF concludes that the evidence is insufficient to determine the balance of benefits and harms of screening mammography in women 75 years or older. [BC2,3]	**Women 40-74 y/o**	Biennial screening mammography
	Women > 75 y/o	Current evidence is insufficient
	Women with dense breasts	Supplementation with USG or MRI- evidence is insufficient
WHO: For well-resourced and limited resource settings with strong health systems: Mammography every 2 years for women 50-69 y/o. In well-resourced settings, WHO suggests an organized, population-based screening program for women aged 40–49 and 70-75 years only if such a program is conducted in the context of rigorous research, monitoring, and evaluation. In limited resource settings with weak or relatively strong health systems, WHO recommends against the implementation of population-based screening programs for women aged 40–49 years. [BC 1]		

Diagnostic Procedures

Standard of Care [BC 2,3]	
Screening: used to detect cancer in asymptomatic women	**Diagnostic evaluation**: to characterize a clinical finding or abnormality found during screening. May include diagnostic mammography, ultrasonography, and at times diagnostic breast MRI.
Biopsy: - Fine needle aspiration - Core needle - Excisional	
Emerging Technologies and Clinical Trials	
A Clinical Investigation to Evaluate Microwave Imaging via MammoWave in a Population- based screening program for Early Breast Cancer Detection. [BC6]	**Remote breast Cancer screening based on automated breast ultrasound** [BC7]
Circulating Tumor Cells Screen for Breast Cancer [BC8]	**iBreast exam- handheld device that performs a painless electronic palpation**. Creates a color map of the breast with red spots indicating areas that could be abnormal. [BC9]
High vs. Low Resource Settings	
High Resource	**Low Resource** Screening is opportunistic

Country-Specific Examples (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil**
United States	**Mozambique**
Country-Specific Unmet Needs (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil**
United States	**Mozambique**
Country-Specific Preferences for POC screening	
Costa Rica	**Brazil**
United States	**Mozambique**

BREAST CANCER

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Skin Cancer

Statistics And Risk Factors [SC 1, 2, 3]
Skin cancer is the most commonly diagnosed cancer in the US. Basal Cell carcinoma and Squamous Cell carcinoma are the most common but rarely lead to death or substantial morbidity. Melanomas represent about 1% of skin cancer but cause the most deaths. Melanoma is 30 times more common in white populations than black populations, but later diagnosed in the black population. In 2022, about 330000 new cases of melanoma were diagnosed worldwide, and almost 60000 people died of the disease. The International Agency for Research on Cancer (IARC) and its partners predict that the number of new cases of cutaneous melanoma per year will increase by more than 50% from 2020 to 2040. US Hispanic and black individuals have worse survival outcomes in cutaneous melanoma than other groups. Melanoma risk factors include male sex, > 50y/o, tendency to sunburn and/or multiple atypical nevi, genetic predisposition, personal and family history, and UV exposure. [SC3]

Screening

Guidelines	
No current USPSTF recommendations for skin cancer screening for adolescents or adults without symptoms. [SC 1]	Australia, New Zealand, Germany, the Netherlands, and the UK recommend screening a certain subset of patients at increased risk for melanoma. [SC2]
A visual skin examination is the most proposed method. [SC1] Only a few professional organizations offer specific statements or recommendations about skin cancer screening; these include the American Academy of Dermatology, the American Cancer Society, the American Academy of Family Physicians and the Skin Cancer Foundation. [SC2,3]	
WHO recommendations: no current guidelines or recommendations for screening.	

Diagnostic Procedures

Standard of Care [SC1,2]	
Visual Skin examination **a. Naked eye** **b. Dermatoscopy**	ABCDE of suspicious lesions: Asymmetry, Border irregularity, color uniformity, diameter (> 6mm), evolution over time.
"Ugly duckling sign": the clinician identifies lesions that look different than other moles on the patient.	Biopsy of suspicious lesions
Emerging Technologies and Clinical Trials	
At-Home Dermoscopy AI for optimizing early triage of Skin Cancers and Atypical Melanocytic Nevi Enables laypersons to triage self-selected pigmented lesions of concern from home. [SC 4]	**DermaSensor Postmarket Surveillance Study** Elastic scattering spectroscopy device uses a spectrum of light reflectance to compare suspicious lesion signatures to that of previously scanned lesions with known benign or malignant pathology. [SC5]
Melanoma Detection in Switzerland with VECTRA (MELVEC) To compare 2D- and 3D-imaging (+AI) and routine clinical care in early melanoma detection in a prospective large-scale real-world data set. [SC6]	**Imaging techniques:** Confocal Microscopy, Optical Coherence Tomography, High-Frequency Ultrasound, Raman Spectroscopy, Fluorescence imaging, Multispectral optoacoustic tomography. [SC7]
Spectrophotometric intracutaneous analysis It involves examining skin hemoglobin and melanin content with software algorithms. [SC7]	

High vs. Low Resource Settings	
High Resource	**Low Resource**
Country-Specific Examples (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil** Hospital de Amor has public campaigns for screening using telemedicine. They set up booths at malls and people can take pictures that are sent to a dermatologist for evaluation and the hospital reaches out to patients with suspicious lesions.
United States	**Mozambique**
Country-Specific Unmet Needs (Screening, Diagnostics, Early Treatment)	
Costa Rica	**Brazil**
United States	**Mozambique**
Country-Specific Preferences for POC screening	
Costa Rica	**Brazil**
United States	**Mozambique**

SKIN CANCER

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Lung Cancer

Statistics And Risk Factors
• Leading Cause of global cancer incidence and mortality. 2.5 M new cases and 1.8 M deaths in 2022 26%- 5-year survival • Contributors: Tobacco 90% [LC 3, 4,6,7] • Over 80% of smokers worldwide reside in LMICs, accounting for more than 70% of all global smoking-related deaths. Non-small-cell lung cancer accounts for approximately 85% of all lung cancers. [LC6]

Screening

Guidelines- [LC 8]

TABLE 1. Lung cancer screening recommendations[5,7-11]

	USPSTF	NCCN	ACS	AATS	CHEST
Age (years)	50-80	55-77	50-80	55-79	55-77
Smoking history (pack-years)	At least 20	At least 30	At least 20	At least 30	At least 30
Smoking status	Current or quit in past 15 years	Current or quit in past 14 years	Current or quit in past 15 years	Not specified	Current or quit in past 15 years
Shared decision-making visit	Required	Required	Required	Not required	Suggested
Other notes		May start at 50 years**	Must receive tobacco cessation counseling	May start at 50 years***	Must be asymptomatic
Method	Low-dose CT	Low-dose CT	Low-dose CT	Low-dose CT	Low-dose CT
Interval	Annual*	Annual	Annual	Annual	Annual****
Last updated	2021	2020	2021	2012	2018

*Stop screening if patient develops a comorbidity that substantially limits life expectancy.
**Start screening at age 50 years and 20 pack-years if the patient also has at least one other risk factor other than secondhand smoke (contact with radon, asbestos, or other cancer-causing agents; history of cancer; family history of lung cancer; history of COPD or pulmonary fibrosis).
***Start screening at age 50 years and 20 pack-years if the patient also has an additional cumulative risk of developing lung cancer of at least 5% over the next 5 years.
****Do not screen if the patient has comorbidities that adversely influence the ability to tolerate screening or treatment of detected lung cancer, or that substantially limit life expectancy.

The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20-pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. [LC1] Screening programs for early detection of lung cancer vary depending on the resources and infrastructure [LC 3,4]
The American Cancer Society recommends annual screening for lung cancer with LDCT in asymptomatic individuals aged 50-80 years who smoke or previously smoked (20 pack-year or more smoking history) [LC 7]

WHO recommendations focus on prevention, by campaigning against tobacco use. [LC10}

Diagnostic Procedures

Standard of Care

The approaches currently used for lung cancer screening include Low-dose CT scans (LDCT), chest X-rays, sputum cytology, biomarker tests, and risk assessment tool rates.[LC 3,4,5,7] LDCT is the gold standard, based on the results from two large randomized clinical trials (NLST and NELSON) showing reduced mortality while the other methods have not been shown to reduce mortality. [LC7,8]

Emerging Technologies and Clinical Trials

Early Cancer Biomarkers in Breath Condensate in high-risk population undergoing LDCT Screening [LC12]	**Assessment of Lung Cancer Risk based on a Biomarker Panel of Circulating Proteins** [LC9]
Feasibility of Cell-Free DNA liquid biopsy in screening High-Risk Patients for Lung cancer [LC11]	

High vs. Low Resource Settings [LC6]

Table 2 | Comparison of US versus LMIC main guidelines

Guidelines	Year	Eligible population				Recommendation	Positive nodule cutoffs
		Age (years)	Pack-years	Quit-years	Considerations		
US							
National Comprehensive Cancer Network (NCCN)	2020	55-77	≥30	≤14	Discontinue if no longer candidate for definitive treatment	Annual LDCT	>5 mm
		≥50	≥20	N/A	Other risk factors[a]		
Screening for Lung Cancer: US Preventive Services Task Force Recommendation Statement[b]	2014	55-80	≥30	≤15	Discontinue if: Limited life expectancy Lack of ability or willingness for curative treatment	Annual LDCT	>5 mm
LMICs							
Recommendations for lung cancer screening in Southern Africa	2019	55-74	≥30	≤15	Discontinue if: Limited life expectancy Lack of ability or willingness for surgery.	Annual LDCT	≥6 mm
China National Lung Cancer Screening Guideline	2018	50-74	≥20	≤5	No history of lung cancer General good health Fit for surgery and willing to further investigate	Annual LDCT	≥5 mm or NCN

Sources: refs. [48,53–55]. N/A, not applicable; NCN, noncalcified nodule. [a]Tobacco smoking; contact with radon, asbestos or other cancer-causing agents; history of cancer, family history of lung cancer; history of COPD or pulmonary fibrosis. [b]The US Preventive Services Task Force Recommendation Statement draft released on 7 July 2020 proposed an updated and broadened eligibility criteria, recommending annual screening for lung cancer with LDCT in adults 50–80 years of age who have a 20-pack-year smoking history and currently smoke or have quit within the past 15 years.

Country-Specific Examples (Screening, Diagnostics, Early Treatment)

Costa Rica	**Brazil**
United States	**Mozambique**

Country-Specific Unmet Needs (Screening, Diagnostics, Early Treatment)

Costa Rica	**Brazil**
United States	**Mozambique**
Country-Specific Preferences for POC screening	
Costa Rica	**Brazil**
United States	**Mozambique**

LUNG CANCER

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Glossary

CITEC	Center for Innovation and Translation of Point of Care Technologies for Equitable Cancer Care
POC	Point of Care
SOC	Standard of Care
GMI	Global Medical Innovation
HPV	Human Papillomavirus
EBV	Epstein Barr Virus
WHO	World Health Organization
MDACC	MD Anderson Cancer Center
BE	Barrett's Esophagus
cfDNA	Circulating free DNA
NGS	Next-Generation Sequencing
gFOBT	Guaiac Fecal Occult Blood Test
FIT	Fecal Immunochemical Test for Hemoglobin
HRA	High-Resolution Anoscopy
HIV	Human Immunodeficiency Virus
USPSTF	United States Preventative Task Force