

To view an archived recording of this presentation please click the following link:

<https://youtu.be/pVMqFOG7bMU>

Please scroll down this file to view a copy of the slides from the session.

#### Disclaimer

**This document was created by its author and/or external organization. It has been published on the Public Health Ontario (PHO) website for public use as outlined in our Website Terms of Use. PHO is not the owner of this content. Any application or use of the information in this document is the responsibility of the user. PHO assumes no liability resulting from any such application or use.**

# Primary and Secondary Prevention of HPV and Anal Cancer



**Ann N Burchell, PhD**  
Canada Research Chair in Sexually  
Transmitted Infection Prevention  
Scientist, Unity Health Toronto  
Professor, Department of Family and  
Community Medicine, Temerty Faculty  
of Medicine, University of Toronto

**Devan Nambiar, MSc**  
Senior Lead, KTE and Science  
Gay Men's Sexual Health Alliance  
(GMSH)



## **Disclosure – Ann Burchell**

- I do not have any relationship with for-profit organizations
- I do have relationships with not-for-profit organizations
  - International Papillomavirus Society – Member of Board of Directors
  - International Anal Neoplasia Society – Member of Implementation Task Force

## **Disclosure – Devan Nambiar**

- I do not have any relationship with for-profit organizations
- I do have a relationship with not-for-profit organizations
  - CIHR Pan-Canadian Network for HIV/AIDS & STBBI Clinical Trials Research-Community Co-Lead Cures and Immunotherapies
  - Chair of Community Advisory Board for ACCESS Study (Anal Cancer Equity in screening Services)

## **Disclaimer**

This presentation was created by its authors

It will be published on the Public Health Ontario (PHO) website for public use as outlined in our Website Terms of Use

PHO is not the owner of this content. Any application or use of the information in this document is the responsibility of the user

PHO assumes no liability resulting from any such application or use

# Acknowledgements

## HPV-SAVE Team

Irving Salit  
Troy Grennan  
Ann Burchell  
Jennifer Gillis  
Ramandip Grewal  
Gina Ogilvie  
Mark Gaspar  
Daniel Grace  
Aisha Lofters  
Janet Raboud  
Olli Saarela  
Paul MacPherson  
Ron Rosenes

## HPV Women's Team

Ann Burchell  
Jennifer Gillis  
Joanne Lindsay  
Anita Benoit  
Catharine Chambers  
Claire Kendall  
Abigail Kroch  
Ramandip Grewal  
Mona Loutfy  
Ashley Mah  
Kristen O'Brien  
Gina Ogilvie  
Janet Raboud  
Anita Rachlis  
Beth Rachlis  
Anna Yeung  
Mark Yudin

## ACCESS Study Team

Ann Burchell  
Christine Fahim  
Gordon Arbess  
Joshua Edward  
Daniel Grace  
Rachel Leggett  
Paul MacPherson  
Mary Ndung'u  
Irving Salit  
Kevin Woodward  
Rose Zaranyika

Troy Grennan  
Meghan Walker  
Tyler Chesney  
Dina Gaid  
Daniel Kurani  
Aisha Lofters  
Devan Nambiar  
Apondi Odhaimbo  
Michael Silverman  
Anna Yeung

- OHTN Cohort Study participants
- OHTN Cohort Study investigators, sites, staff, committees
- ESTIMATE Lab staff and trainees
- Community Advisors
- Research Funders and Collaborators



ACCESS



# Learning Objectives

1

Explain clinical and epidemiological background of HPV infection and anal cancer

2

Describe risk factors for anal cancer

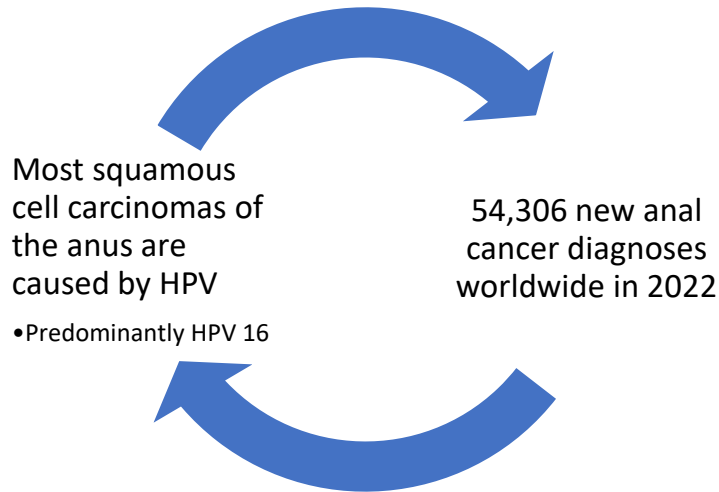
3

Consider implementation needs for anal cancer screening

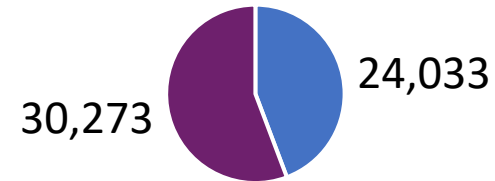
4

Develop competencies to discuss HPV and anal cancer with patients and with medical professionals

# Anal cancer is rare in the general population



## Global anal cancer, 2022



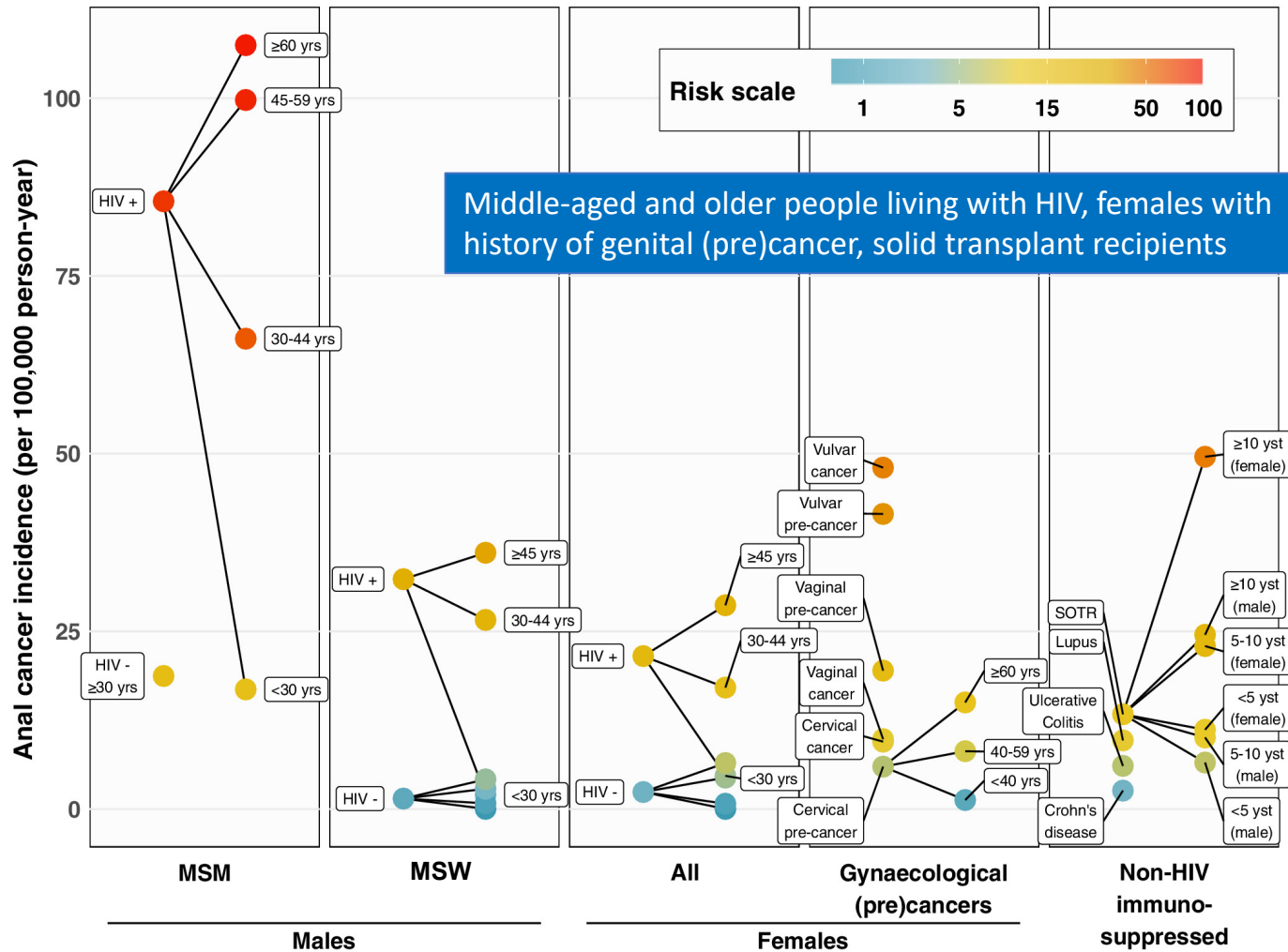
■ Males ■ Females

**0.51 per 100,000**    **0.57 per 100,000**

De Martel et al. *Lancet Global Health* 2020.

Deshmukh et al. *Int J Cancer* 2023.

GLOBOCAN 2022. Global Cancer Observatory, <http://gco.iarc.fr/>



Rates of anal cancer risk are higher among people with a compromised immune status, including people living with HIV, with risk rising with age

Clifford et al.  
*Int J Cancer* 2020;  
 148(1): 38-47.

Cumulative risk for anal cancer by age 65 in Ontario,  
2012-2020 (95% confidence interval)

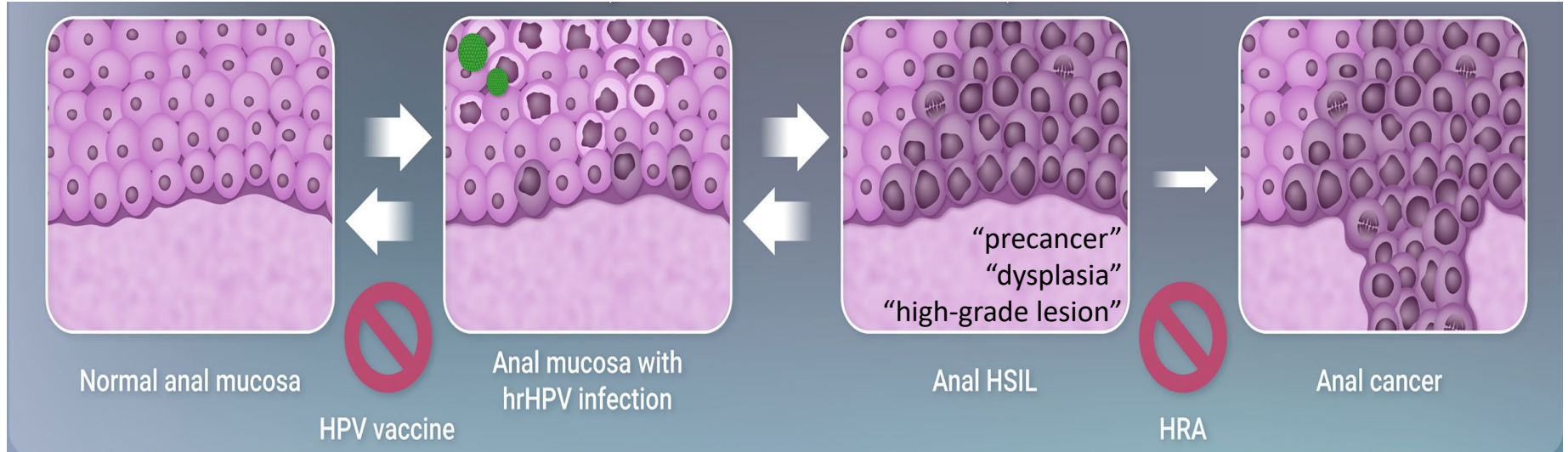
People living with HIV

1.8% (1.3, 2.3%)

People not living with HIV

0.02% (0.0, 0.1%)

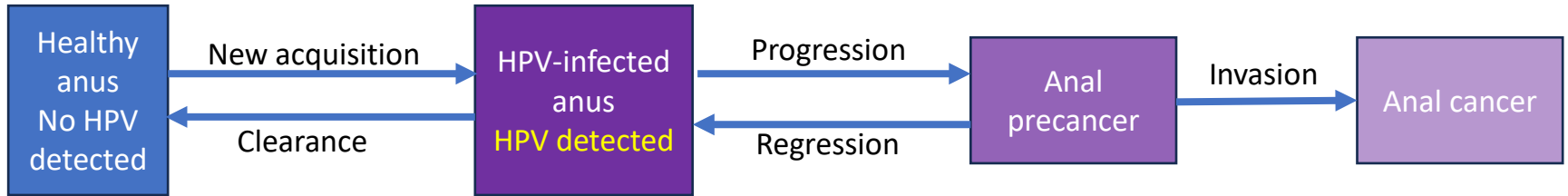
Over a period of years, HPV infection can cause changes to the cells lining the anal canal that can progress to a high-grade intraepithelial lesion (HSIL) and eventually to anal cancer



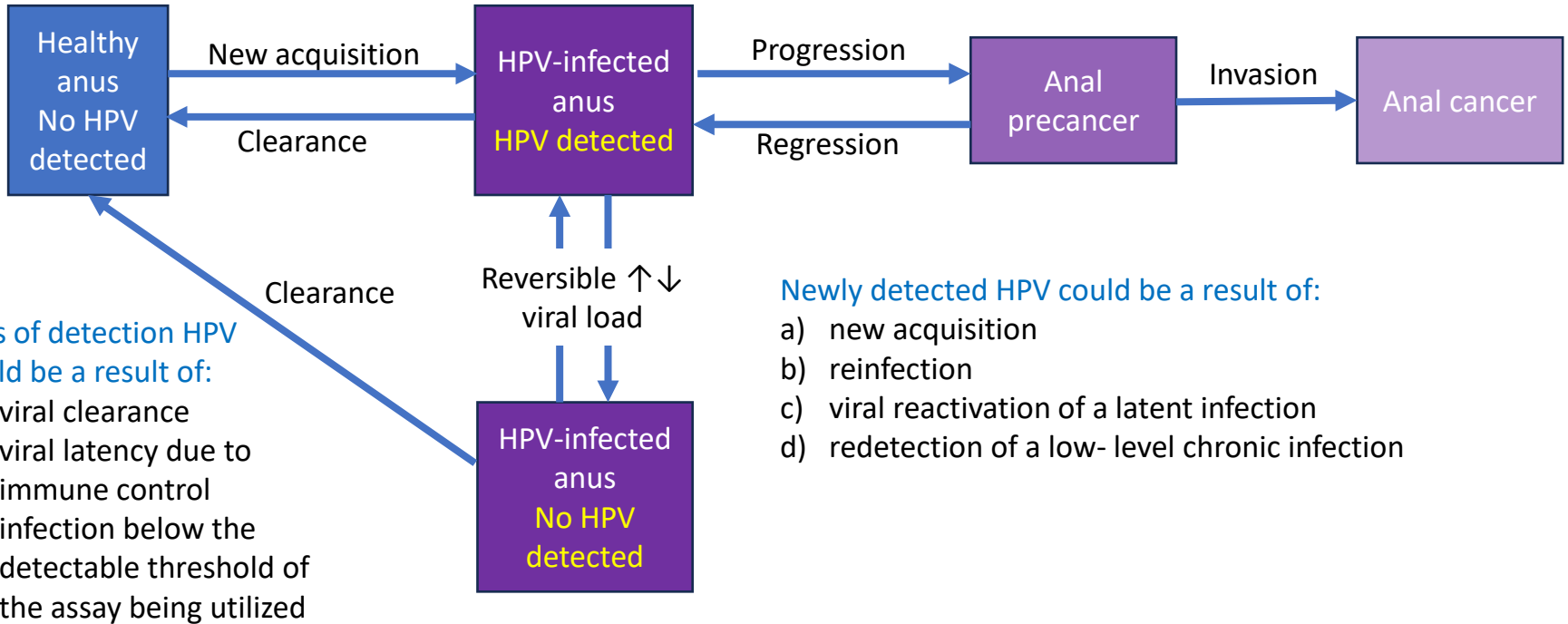
**HPV vaccination** prevents infection in the first place

**Anal cancer screening** aims to detect lesions and treat them before progression to cancer, or to detect cancer at earlier stages when it is easier to treat

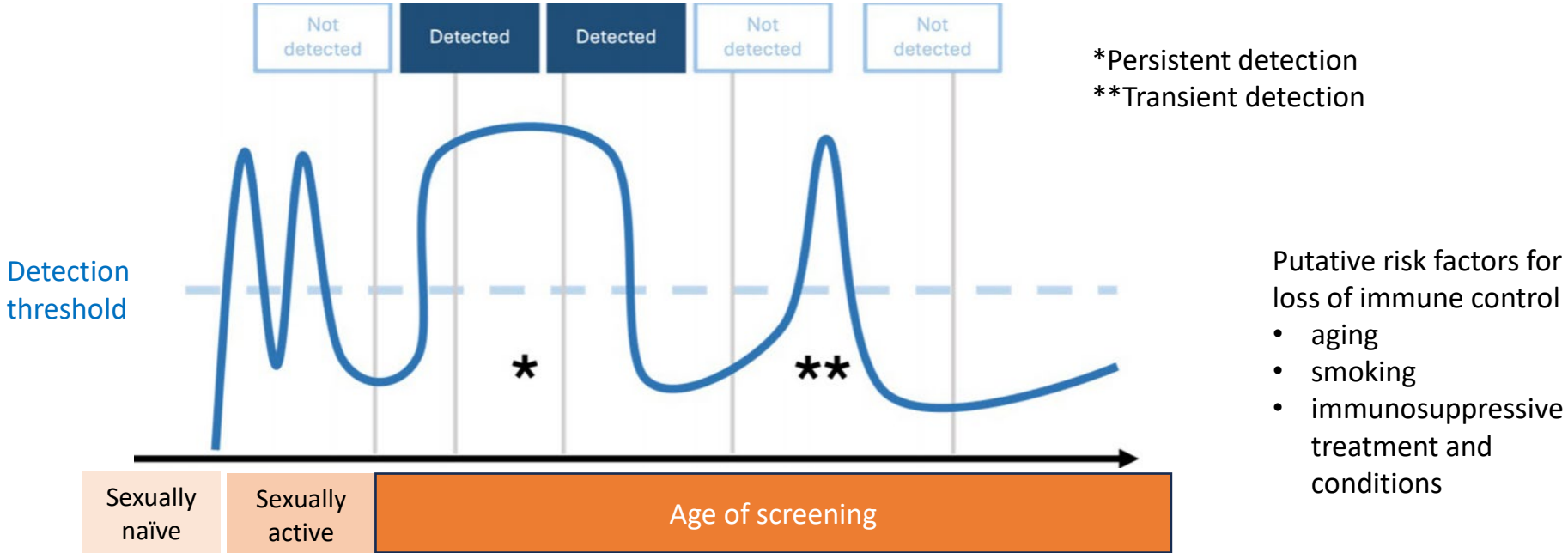
# Updated natural history of HPV and cancer



# Updated natural history of HPV and cancer



# HPV acquired at a younger age can persist over the lifespan and be intermittently detectable



Lyke, ..., IPVS Policy Committee. *Am J Obstetrics Gynecology* 2025; 232(5):453-60.

# What about HPV vaccine?

---

Evidence to support primary prevention of anal cancer



Photo credit: University of Arkansas for Medical Sciences (UAMS) News

# Evidence for HPV vaccine benefit against...

- **Prevalent and incident anal HPV** in trials in less exposed populations
- **Prevalent and incident anal HPV** in real-world populations among youth and young adults, primarily HIV-negative
- **Persistent anal HPV** in trials in less exposed populations
- **AIN/HSIL** in trials in primarily unexposed populations, including those living with HIV

Kreimer et al. *Lancet Oncol* 2011; 12:862-70

Palefsky et al. *NEJM* 2011

Wilkin et al. *Clin Infect Dis* 2018

Palefsky et al. *Clin Infect Dis* 2021

Wei et al. *J Infect Dis* 2023; 228:1496-504.

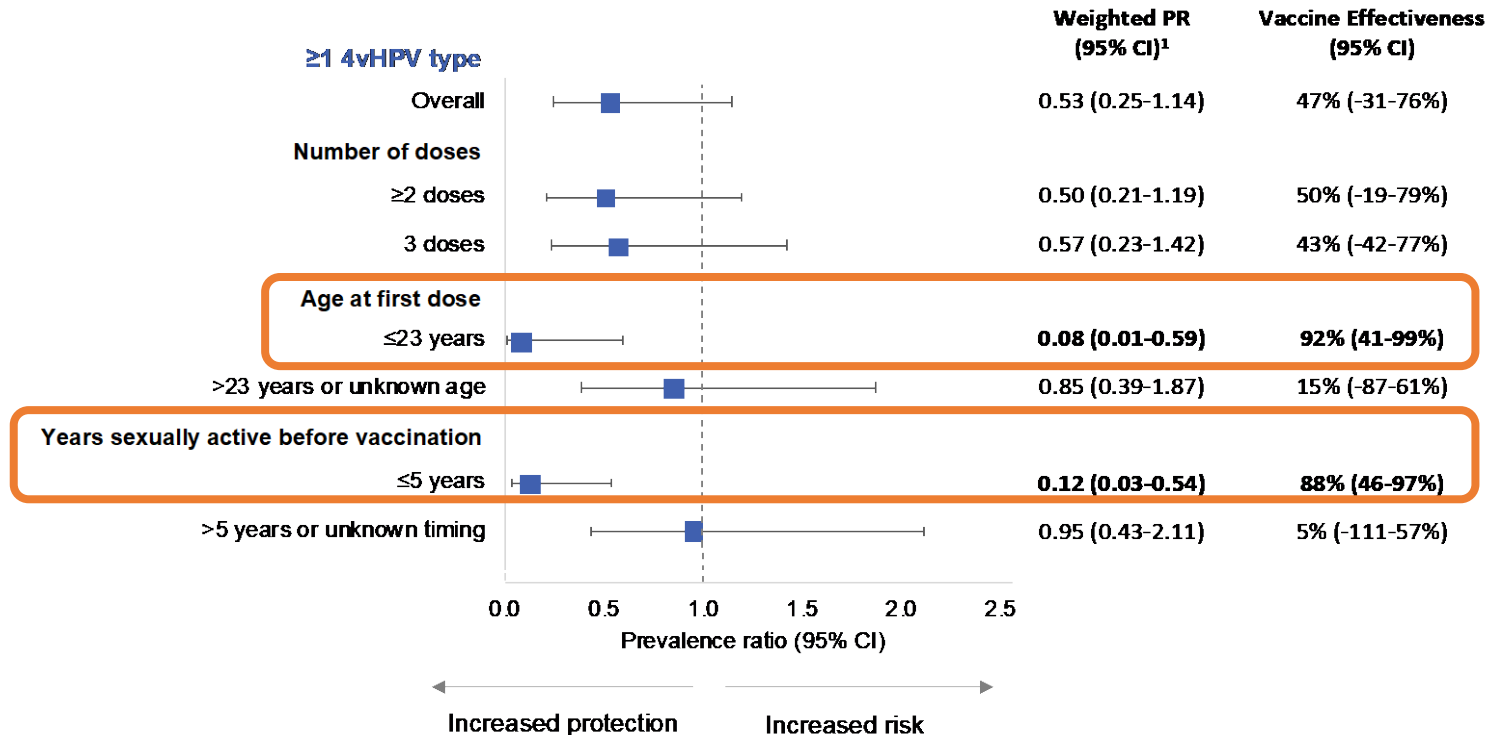
**Less exposed =**

Younger

Fewer lifetime sexual partners

Seronegative for HPV types at study entry

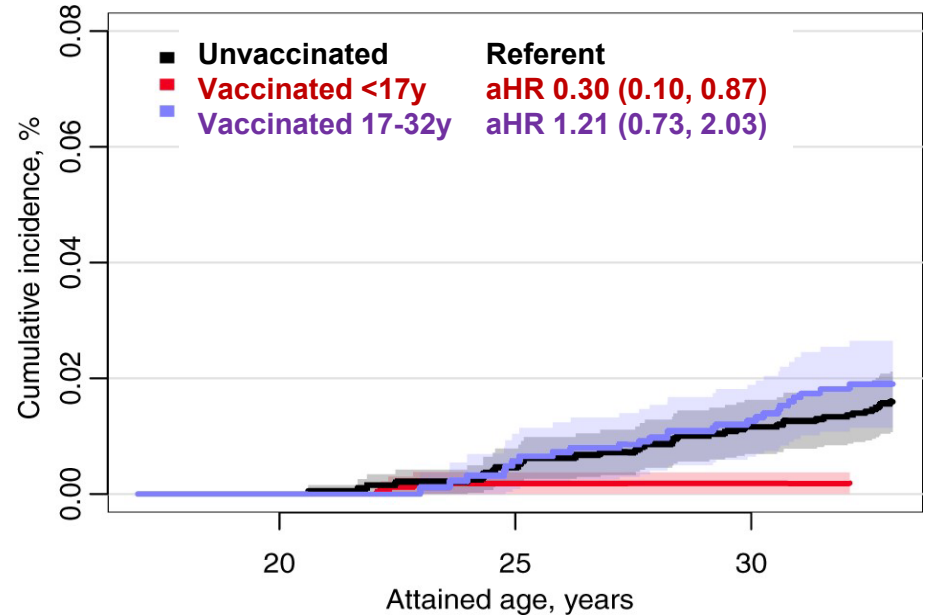
# Real-world evidence for benefit against 12-month persistence of anal 4vHPV among sexual minority men when received at 23 years or younger or within 5 years of first anal sex encounter



# First real-world study to demonstrate HPV vaccine effectiveness against anal HSIL



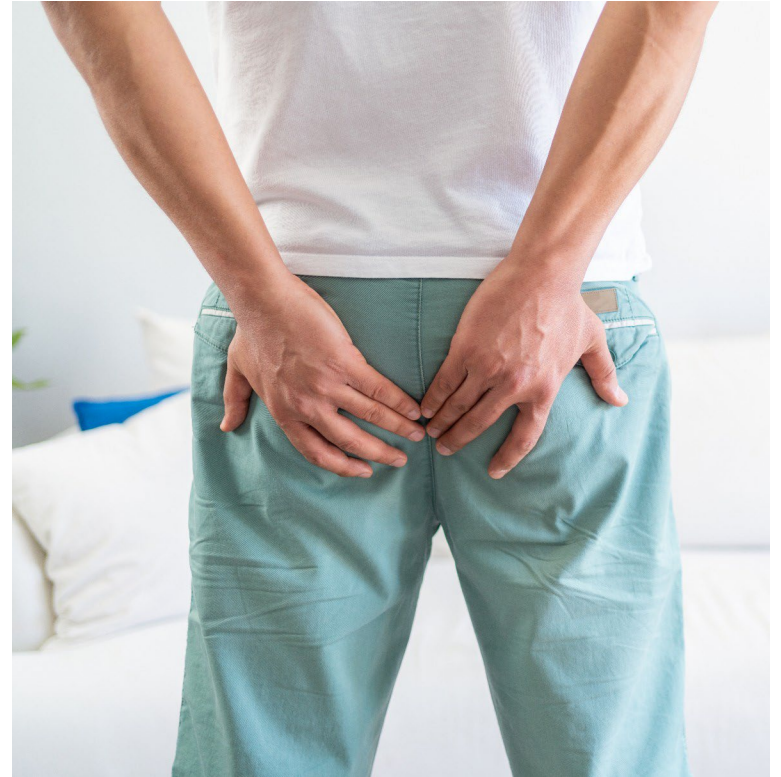
- Nationwide cohort of all Danish women aged 17-32 years, 2006-2021
- 1-dose HPV vaccine effectiveness against first occurrence of anal HSIL or worse
- Adjusted for age and education (individual/parental)
- **70% lower hazard of anal HSIL or worse if vaccinated under the age of 17 years**



# Why screen?

---

Evidence to support detection and treatment





the  
**ANCHOR**  
study.org

## Anal Cancer HSIL Outcomes Research

- **Design:** Phase 3 randomized controlled trial at 25 sites in the United States and Puerto Rico
- **Population:** 4446 adults living with HIV who had biopsy-confirmed high-grade squamous intraepithelial lesions (HSIL) enrolled from 2014 to 2021
- **Intervention:** immediate treatment until complete resolution (office-based ablation, ablation or excision under anesthesia, or topical therapies)
- **Control:** active monitoring without treatment
- **Outcome:** progression to anal cancer
- **Time:** evaluated every 6 months



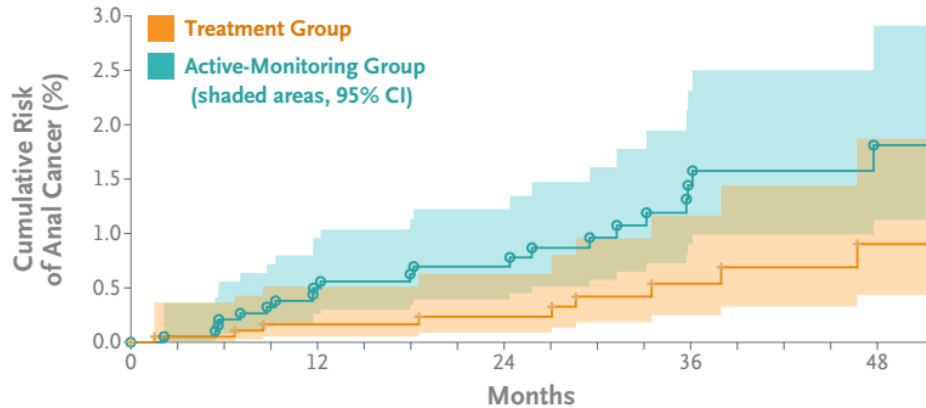
the  
**ANCHOR**  
study.org

## Anal Cancer HASIL Outcomes Research

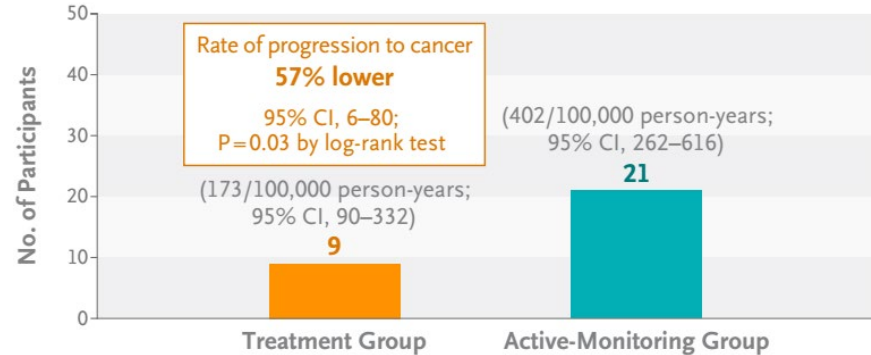
- Trial stopped after an interim analysis demonstrated benefit
- Treatment offered to all in the active monitoring arm

### Time to Progression to Anal Cancer

P=0.03 by log-rank test

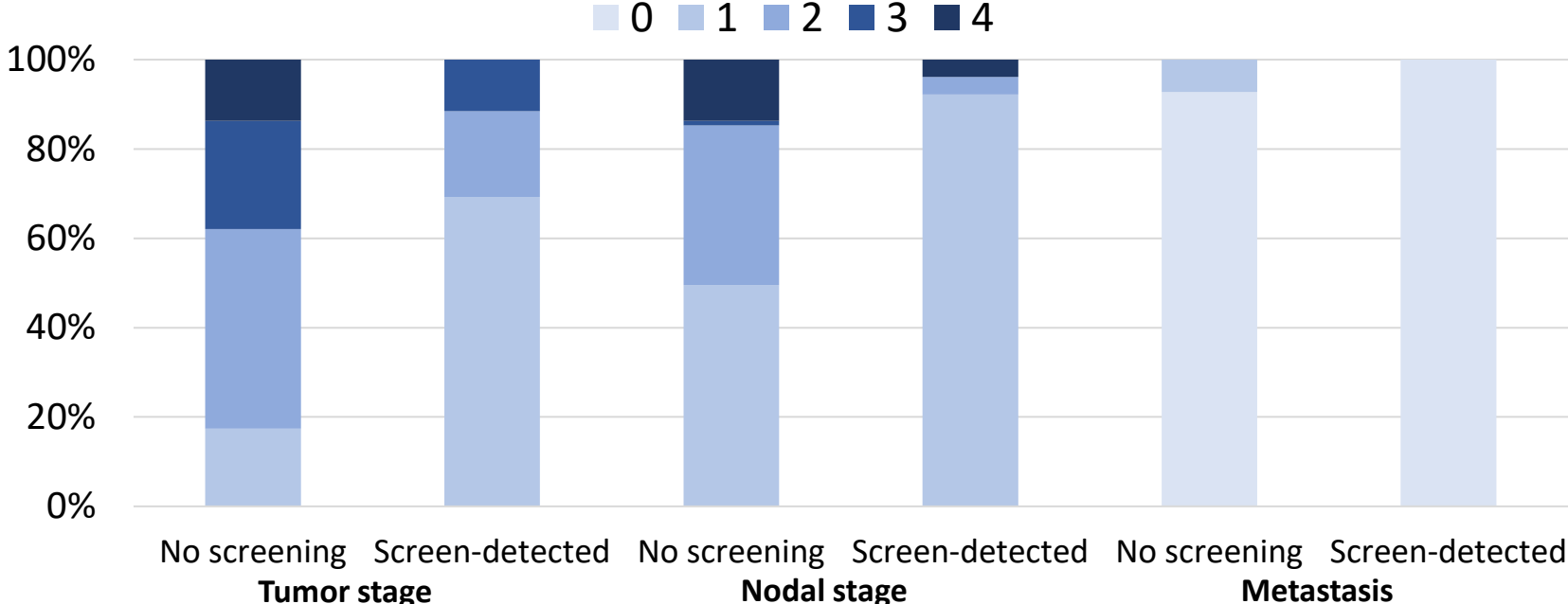


### Invasive Anal Cancer (Median Follow-up, 25.8 Mo)



# Screen-detected anal cancers tend to be detected at earlier stage, less complicated treatment

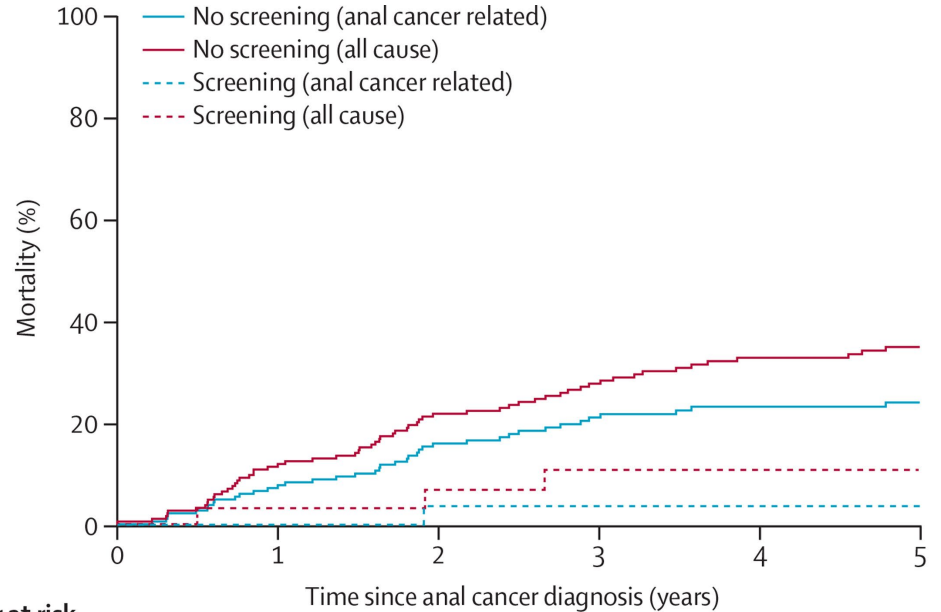
612 squamous cell carcinoma of the anus (26 screen-detected), Toronto, Canada, 2002 to 2022



Walker et al. *Dis Colon Rectum* 2024; 67:32-41.

# Anal cancer-associated mortality is higher in unscreened compared to screened individuals

Men living with HIV in the AIDS Therapy Evaluation in the Netherlands (ATHENA) Cohort, 1996 to 2020



	Number at risk					
	0	1	2	3	4	5
No screening (anal cancer related)	187 (0)	163 (11)	141 (18)	120 (31)	100 (48)	88 (147)
No screening (all cause)	187 (0)	163 (3)	141 (6)	120 (17)	100 (29)	88 (126)
Screening (anal cancer related)	30 (0)	29 (1)	26 (3)	22 (7)	17 (12)	12 (29)
Screening (all cause)	30 (0)	29 (0)	26 (2)	22 (5)	17 (10)	12 (27)

van der Zee et al. *Lancet HIV* 2023; 10:e97-106.

# Who and how to screen?

---

Recommended populations, screening tests, and referral for confirmatory testing with high resolution anoscopy (HRA)



# International / National anal screening guidelines

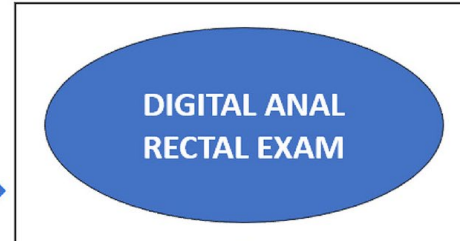
Target populations for screening	U.S. National Institutes of Health Office of AIDS Research	Brazilian Society of Surgical Oncology	Portuguese Society of Colproctology	French National Society of Colproctology	Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine	International Anal Neoplasia Society
MSM living with HIV	●	●	●	●	●	●
Transgender women living with HIV	●				●	●
Transgender men living with HIV	●				●	●
Cisgender women living with HIV	●				●	●
MSW living with HIV	●				●	●
Women with solid organ transplant >10 years			●	●		●
Men with solid organ transplant >10 years						●
Women with vulvar (pre)cancer			●	●		●
MSM / transgender women living with HIV						●

Albuquerque et al. *J Lower Genital Tract* 2025; 29(2):180-5.  
[www.ashm.org](http://www.ashm.org), released March 2025

MSM, men who have sex with men  
 MSW, men who have sex with women

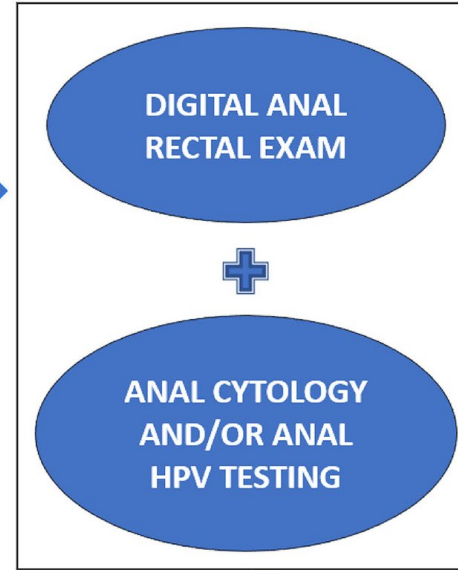
# What is the screening procedure?

SCREENING FOR  
EARLY STAGE  
ANAL CANCER



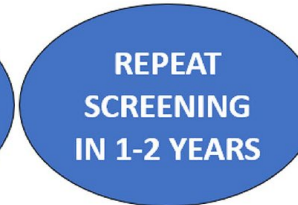
# What is the screening procedure?

SCREENING FOR  
EARLY STAGE  
ANAL CANCER



Abnormal  
Result

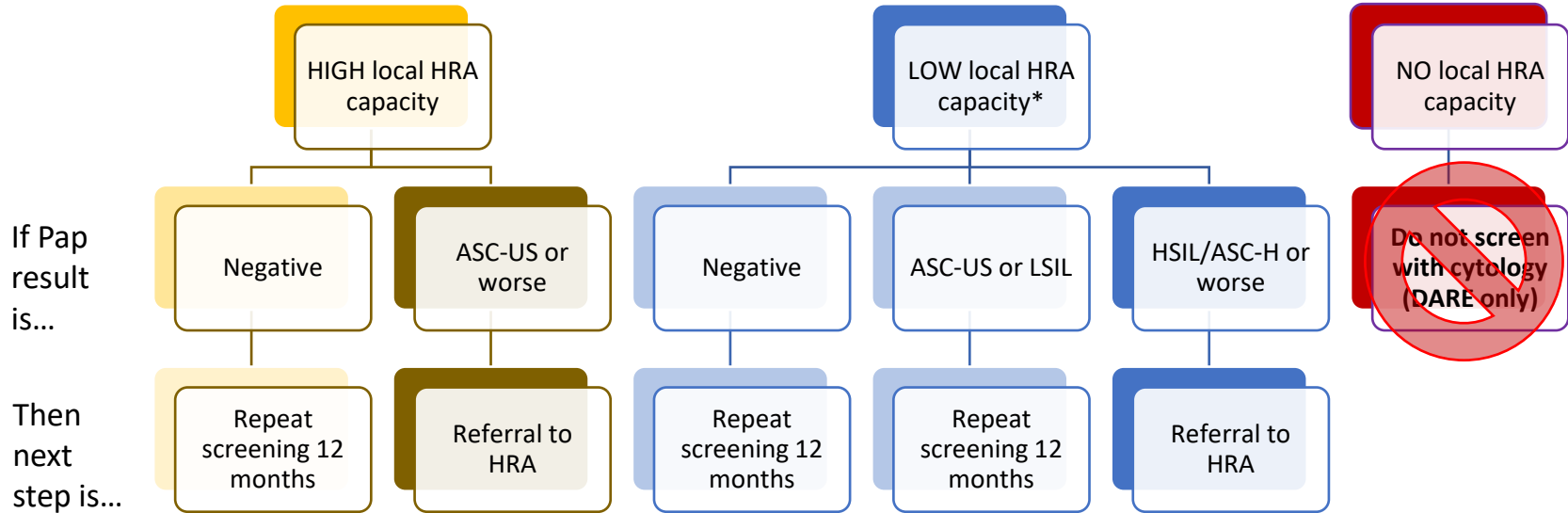
Normal  
Result



SCREENING FOR  
ANAL PRE-CANCER

Recommended  
only if there are  
available  
specialists to  
refer for  
confirmatory  
testing with  
high-resolution  
anoscopy  
("HRA")

IANS guidelines for use of **cytology screening test** for anal precancer and management of results with referrals to high resolution anoscopy (HRA)



Stier et al. *Int J Cancer* 2024 May; 154(10):1694-1702. Online: Jan 31, 2024.

\***Low HRA capacity** is defined as greater than 6-month wait for HRA referral for an abnormal screening test

# Screening test performance using triage testing: People living with HIV

Testing strategy	HRA referral threshold	HRA referral rate / Positivity	Sensitivity for HSIL/AIN2+	Specificity for HSIL/AIN2+
Cytology alone	<ul style="list-style-type: none"> <li>• ASCUS+</li> </ul>	76%	86%	31%
Cytology with HPV triage	<ul style="list-style-type: none"> <li>• ASC-H/HSIL regardless of HPV</li> <li>• ASCUS+ &amp; HR-HPV</li> </ul>	65%	83%	49%
HPV alone	<ul style="list-style-type: none"> <li>• HR-HPV</li> </ul>	81%	96%	29%
HR-HPV with cytology triage	<ul style="list-style-type: none"> <li>• HPV-16 regardless of cytology</li> <li>• HR-HPV &amp; ASCUS+</li> </ul>	70%	88%	43%

Gaisa et al. *Clin Infect Dis* 2025; 81(2):345-347.

# Predicting and Evaluating Anal Cancer in HIV: The PEACH Study



- Observational study to recruit people living with HIV in Vancouver and Toronto
  - GBM and transgender women aged 35+
  - Others living with HIV aged 45+
- Exploring biomarkers beyond cytology and HPV testing for anal screening
- **Aim:** to better predict who is at higher risk of having or developing anal HSIL for more efficient HRA referrals
  - Cytology
  - p16-Ki67 dual stain (cytology)
  - HPV genotyping
  - E6/E7 mRNA expression
  - HPV viral load
  - Circulating tumour DNA (ctDNA)

# Implementation of anal screening

---

What are the challenges and  
opportunities?



# **Anal cancer screening cascade**

# Anal cancer screening cascade

Which populations

to screen?

How often?

What is

acceptable?

Who to

prioritize?

Whose clinical

role?

What screening

test? Modality?

Which abnormal

screen test results to

prioritize/refer for high

resolution anoscopy

(HRA)?

What are the wait

times for HRA?

Who attends HRA

and treatment?

What treatment?

How long to

monitor?

# Population of people living with HIV in Ontario



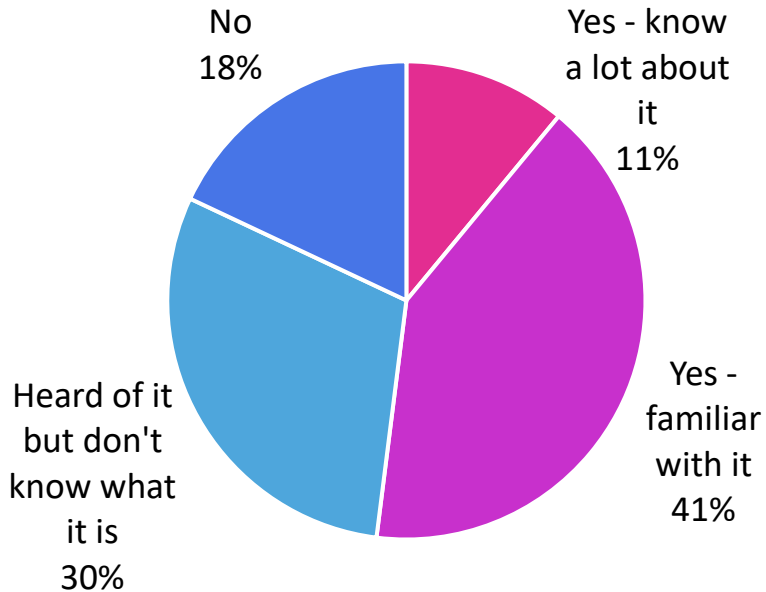
~23,500 adults  
living with HIV

1 in 5 are women

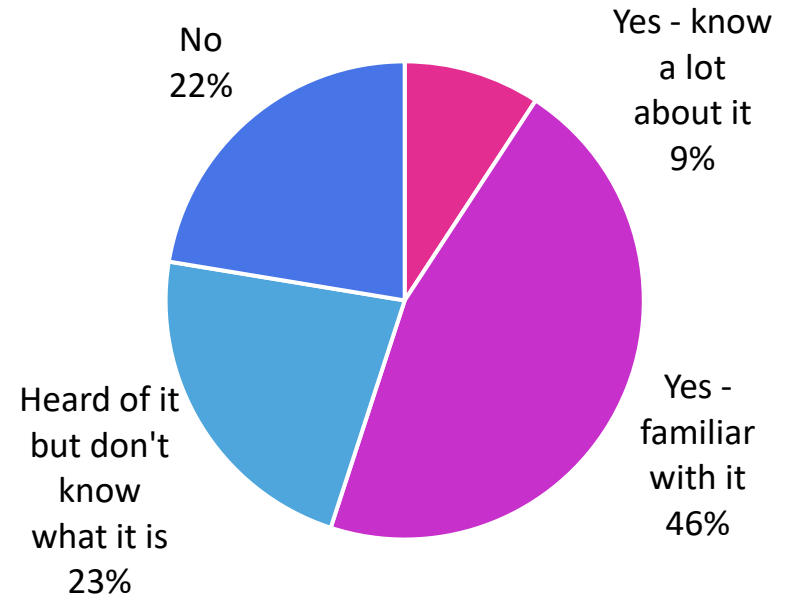



# Have you heard of the human papillomavirus or “HPV”?

**Men living with HIV (n=1677, 2016-17)**



**Women living with HIV (n=670, 2018-20)**

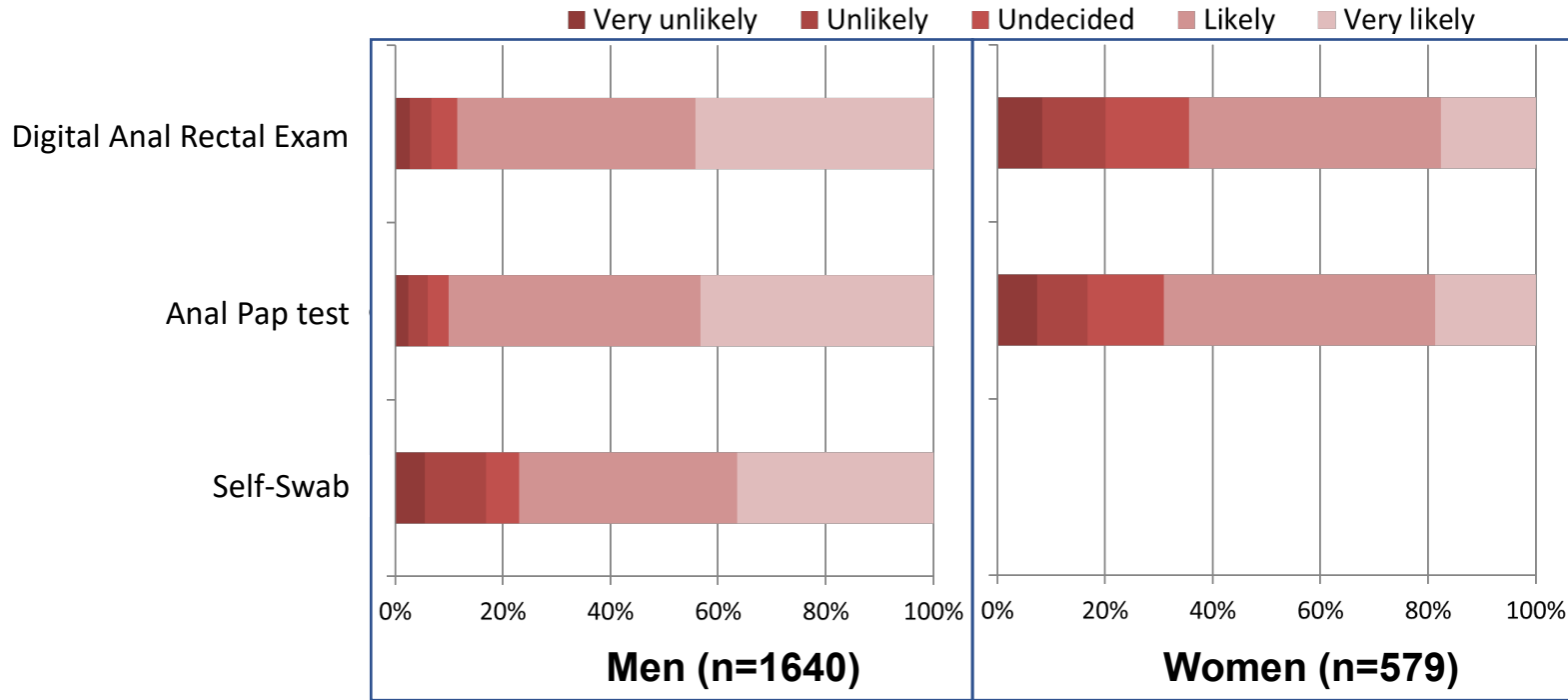




*We asked :*  
In your lifetime,  
what do you think  
your chance is of  
getting **anal cancer**?

**71% of men and 75%  
of women said they  
had “no chance” or  
“low chance”**

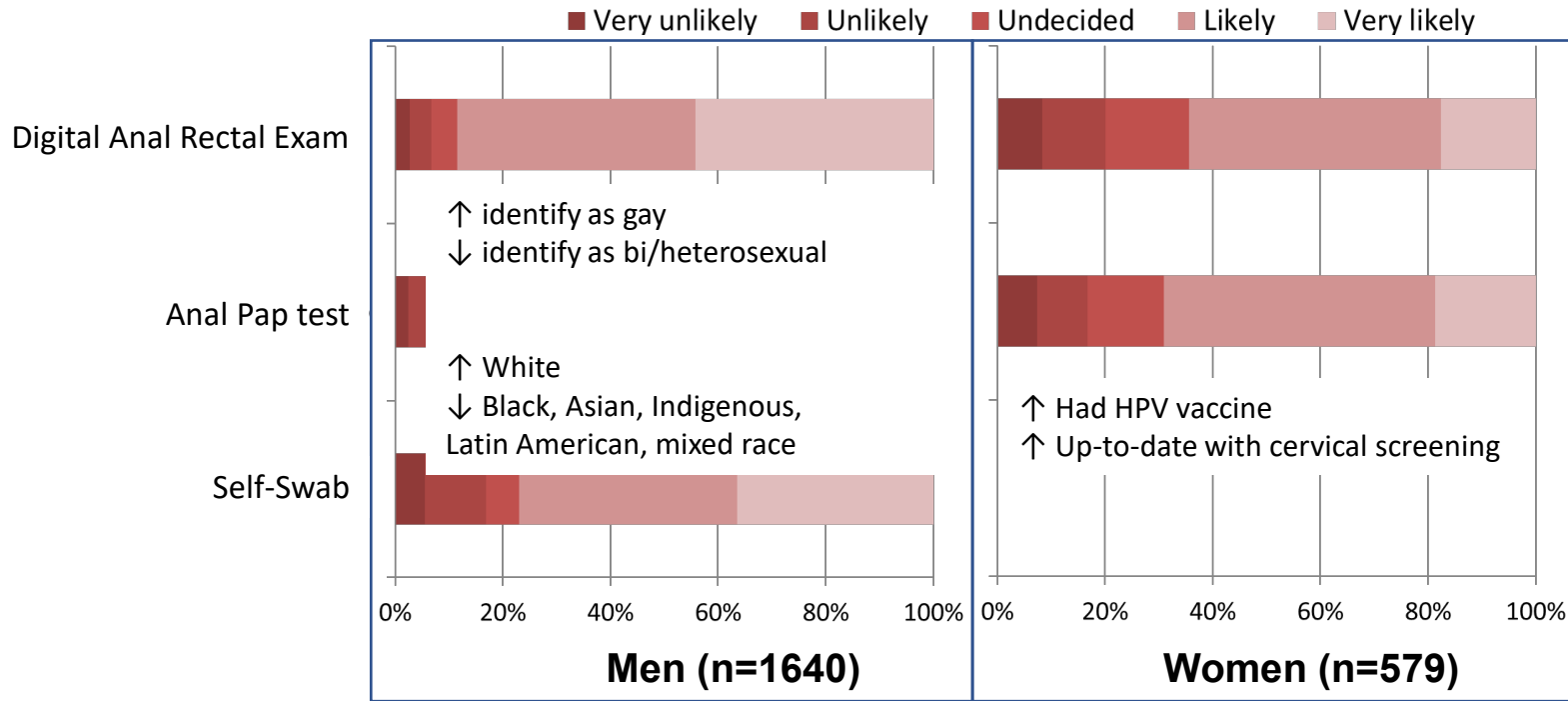
# Willingness among people living with HIV to undergo anal screening in the next year, if offered, Ontario, Canada (Men: 2016-2017; Women: 2017-2020)



Gillis, ..., Burchell. *BMC Public Health* 2022.

Burchell. Unpublished data.

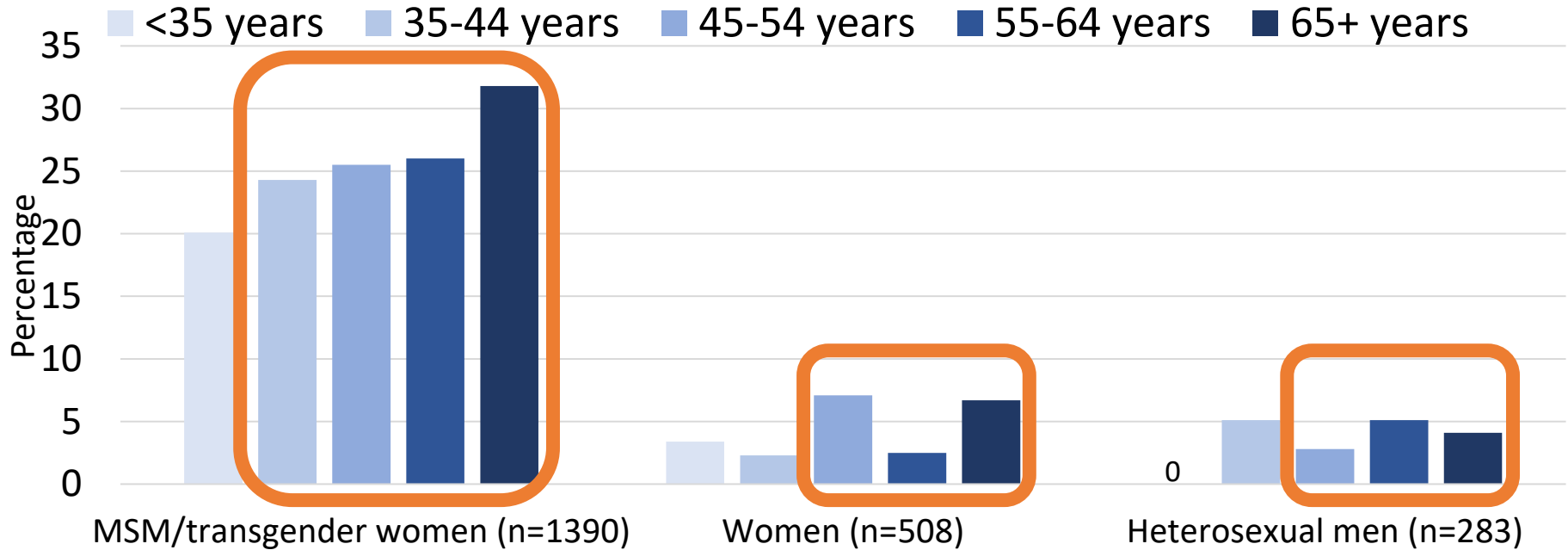
# Willingness among people living with HIV to undergo anal screening in the next year, if offered, Ontario, Canada (Men: 2016-2017; Women: 2017-2020)



Gillis, ..., Burchell. *BMC Public Health* 2022.

Burchell. Unpublished data.

# Self-reported anal Pap cytology in past 12 months among people living with HIV interviewed in 2023, Ontario (n=2181)



Burchell et al. Unpublished data.

# ACCESS

Anal CanCer Equity in Screening Services  
Study

Needs assessment for  
implementation of anal  
cancer screening in  
Ontario

Qualitative descriptive  
design using key  
information interviews  
using

Consolidated Framework for  
Implementation Research (CFIR)

Theoretical Domains  
Framework (TDF)

## Characteristics of clinicians and health system decision makers (n=28) interviewed November 2024 to May 2025

---

Characteristic	Categories	Proportion
Gender	Female	61%
	Male	39%
Location	Toronto	64%
	Outside Toronto	36%
Role	Physician/Surgeon	53%
	Nurse Practitioner	21%
	Registered Nurse	14%
	Decision-maker	14%
Years of experience	1-5 years	29%
	6-10 years	10%
	10+ years	61%

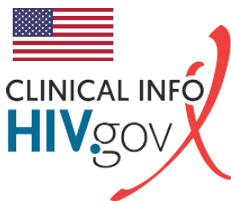
---

Unpublished data.

# ACCESS

Anal CanCer Equity in Screening Services  
Study

What were the opinions  
about the **anal cancer  
screening guidelines?**



- Many expressed **trust** in the guidelines
- Some raised concerns about the strength of the **underlying evidence** and **insufficient contextualization** to the Canadian setting
- Some expressed a need for further direction regarding **which guidelines to follow** in Ontario, or **whether to follow the low- or high-resource setting recommendations**
- More favoured IANS over US HIV guidelines

Unpublished data.

# ACCESS

Anal CanCer Equity in Screening Services  
Study

What were the opinions about the **Ontario setting** for anal cancer screening implementation?

- Uncertainty about **capacity for referrals to HRA specialists** given limited availability
- Concerns about **absence of dedicated physician billing codes**, though some providers rely on alternate codes
- Need for **opinion leaders** and **collaboration with professional bodies** to advocate for implementation

Unpublished data.

# ACCESS

Anal CanCer Equity in Screening Services  
Study

What were the opinions about the **clinical setting** for anal cancer screening implementation?

- Managers/leaders are **generally supportive**
- Screening **aligns with many local priorities**
- Seen as **less relevant** in primary care settings with fewer people living with HIV
- Adoption is **hindered by competing demands, limited time, and heavy caseloads**

Unpublished data.

# ACCESS

Anal CanCer Equity in Screening Services  
Study

What were needs of **individual clinicians** for anal cancer screening implementation?

- Lack of clear **professional boundaries** regarding whose responsibility it is to conduct screening
- Some had **gaps in knowledge**
- Variable **proficiency** and **confidence** conducting digital anal rectal exams (DARE) and anal Paps
- Most **valued** the guidelines, expressed **motivation** and intention to adopt them
- Some expressed **lack of comfort** having discussions about screening with patients
- Many felt they could incorporate some aspects of screening if **training** was available

Unpublished data.

# ACCESS

Anal CanCer Equity in Screening Services  
Study

What were clinicians' opinions about needs for **people living with HIV** and anal cancer screening implementation?

- **Anticipate low acceptability**
  - due to taboos, stigma and shame, past trauma including sexual abuse/assault, perceiving procedure as invasive/uncomfortable
- Concerns about **gender-related barriers**
- **Education** for people living with HIV and the public
- **Partnering with community organizations** that can help raise awareness, do outreach

**COMING SOON!**

Findings from interviews and focus groups with 74 people living with HIV

Unpublished data.

# Resources to support implementation of anal screening

---



# HPV AND ANAL CANCER SCREENING

Men who have sex with men (MSM) and trans women, and particularly older people living with HIV in these groups, are much more at risk than the general population to get anal cancer from HPV infection.

## HPV OVERVIEW:

HPV is a group of over 200 viruses that can cause warts and cancer

## TRANSMISSION:

HPV spreads through sexual (e.g. vaginal, anal, oral) and non-sexual contact (e.g. sharing personal items), and affects nearly all sexually active people over their lifetimes.

## RISK GROUPS:

MSM, trans women, and people living with HIV (PLHIV) are amongst populations at a higher risk for HPV-related anal cancer.

## CANCER DEVELOPMENT:

High-risk HPV strains can cause abnormal cell changes (dysplasia), possibly progressing from precancerous lesions to cancer if untreated.

## SYMPTOMS:

High-risk HPV may remain symptomless for years until cancer develops, while low-risk HPV may cause warts on or around the genitals, anus, or throat.

## SCREENING METHODS:

Key screening options include Digital Anal Rectal Examination (DARE), anal Pap smears, and high-resolution anoscopy (HRA); guidelines recommend screening certain groups, including MSM, trans women, and PLHIV, starting at age 35-45 years.

## TREATMENT OPTIONS:

HPV-related conditions are treated case by case; wart treatment includes freezing therapy (liquid nitrogen), topical medications, and surgery, while precancerous lesions may be treated similarly or may be treated using laser or electrocautery therapy.

## VACCINE:

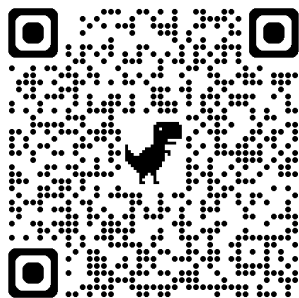
The Gardasil® 9 (HPV9) vaccine protects against 9 common HPV types, recommended for individuals aged 9-45, with the greatest benefit in those 9-26.

## RISK FACTORS FOR ANAL CANCER:

Risk factors include smoking, multiple sexual partners, receptive anal intercourse, aging, and immunosuppression (e.g., organ transplants).

## SEXUAL HEALTH:

Open conversations about sexual practices and risk reduction are essential for anal cancer prevention.



MAIN MENU

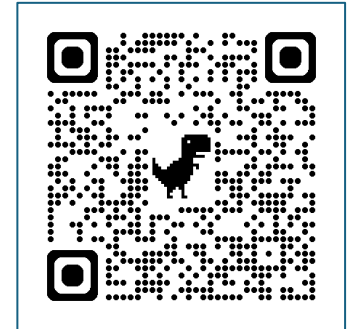
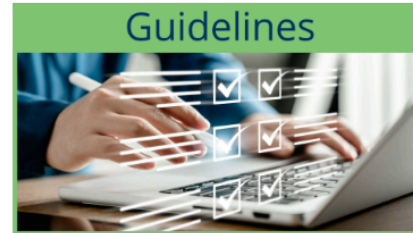
## Anal Cancer Prevention Screening Toolkit

### INTRODUCTION

Anal cancer prevention begins with screening, with the goal of identifying individuals with anal high-grade squamous intraepithelial lesions (HSIL), the precursor to anal cancer. HSIL is typically diagnosed during evaluation with high-resolution anoscopy (HRA). When HSIL is identified, it can be treated to prevent progression to cancer.

For patients without access to HRA, screening to identify possible anal cancers can be performed using a digital anal rectal examination (DARE), which aims to detect cancers at an earlier and more treatable stage.

This toolkit, developed by the IANS Implementation Task Force, is designed to inform, guide, and support efforts to implement effective anal cancer screening and prevention. The



# ACCESS

Anal CanCer Equity in Screening Services  
Study

**CEP**

Centre  
for Effective  
Practice



# Clinician Toolkit adapted for Ontario

Supporting Anal Cancer Screening in Primary Care for People Living with HIV

Search Content 🔍

What we are screening for

Who to screen

High Resolution Anoscopy

Why is screening needed?

Recognizing and responding to symptoms

What to say: Education and engaging patients in screening

Preparing to screen

How to screen: Recommended practices

What to do next: Referral and follow-up

Additional Resources

# Training in high-resolution anoscopy (HRA)?

## Recommendations from IANS practice standards

- Basic HRA course
- Observation of experienced HRA practitioner
- Preceptorship—expert observation of practice as part of training program
- Mentorship with identified experts
- Regular patient feed-back

**2-5 years to become proficient**

### **Keys to success**

- willingness
- persistence
- multidisciplinary team
- adequate equipment
- institutional support
- volume of cases

# Concluding thoughts

- Prevention of anal HPV infection and anal pre-cancer is possible via HPV vaccination when received before or soon after sexual debut
- Anal cancer screening now recommended for populations at elevated risk, including people living with HIV
- Making it part of routine preventive care will benefit from evidence-informed strategies to support implementation
- For many people living with HIV in Ontario, anal cancer screening will be a new experience
- Health system change is needed to build capacity to offer screening, confirmatory testing, treatment and follow-up care
- Community initiatives to improve participation will ideally include education and messaging that de-stigmatizes anal cancer screening as part of routine HIV care