

Anal cancer prevention for people living with HIV: Current and upcoming strategies

Ann Burchell, PhD,

Canada Research Chair in Sexually Transmitted Infection Prevention

Scientist, ESTIMATE Lab, MAP Centre for Urban Health Solutions, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Unity Health Toronto

Associate Professor, Dept of Family and Community Medicine, Temerty Faculty of Medicine, University of Toronto

Ontario HIV Clinic Education Day

September 28, 2023



ST. MICHAEL'S
UNITY HEALTH TORONTO



UNIVERSITY OF
TORONTO

Acknowledgements

Cancer Burden Team

Ann Burchell
Ioana Nicolau
Tony Antoniou
Jennifer Brooks
Curtis Cooper
Michelle Cotterchio
Claire Kendall
Abigail Kroch
Joanne Lindsay
Anthony Mohamed
Rahim Moinheddin
Colleen Price
Kate Salters
Marek Smieja

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
Abby 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
Troy Grennan
Meghan Walker
Gordon Arbess
Tyler Chesney
Christine Fahim
Daniel Grace
Charlie Guiang
Tae Hart
Aisha Lofters
Paul MacPherson
Devan Nambiar
Mary Ndung'u
Apondi Odhaimbo
Ron Rosenes
Irving Salit
Michael Silverman
Kevin Woodward

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



Today's Aim: To share knowledge regarding

Cancer burden among people living with HIV in Ontario

Anal cancer risk and knowledge among people living with HIV

Existing and new tools for anal cancer prevention

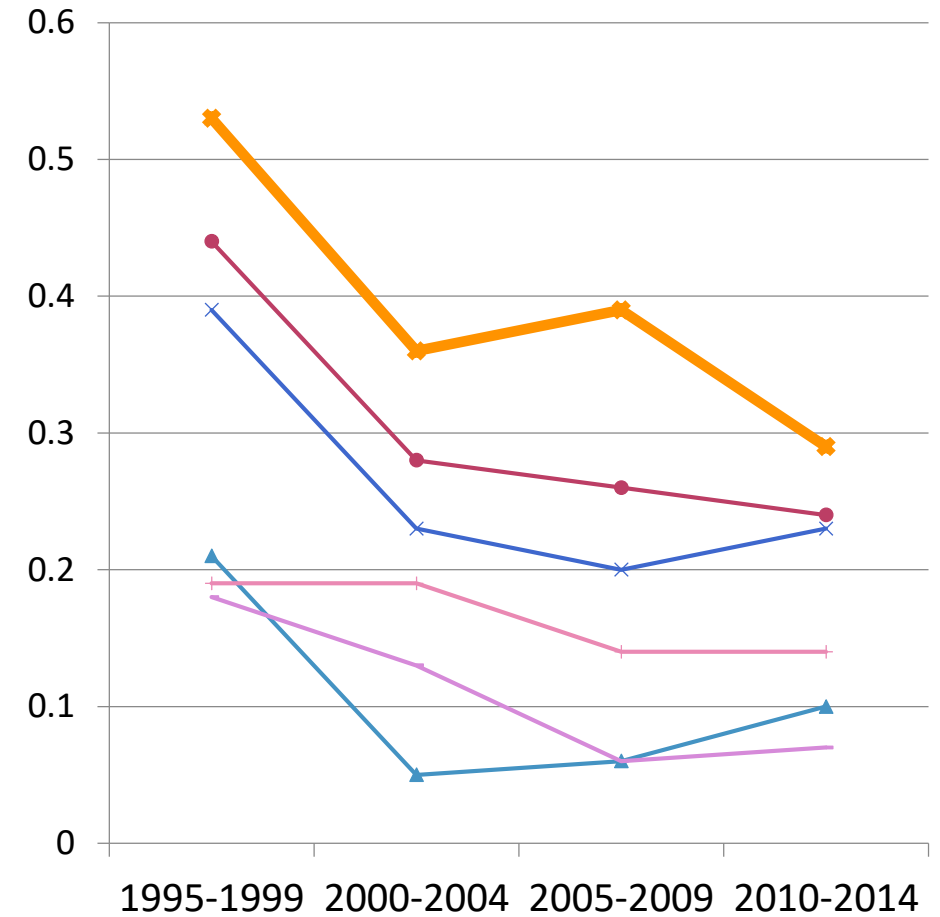
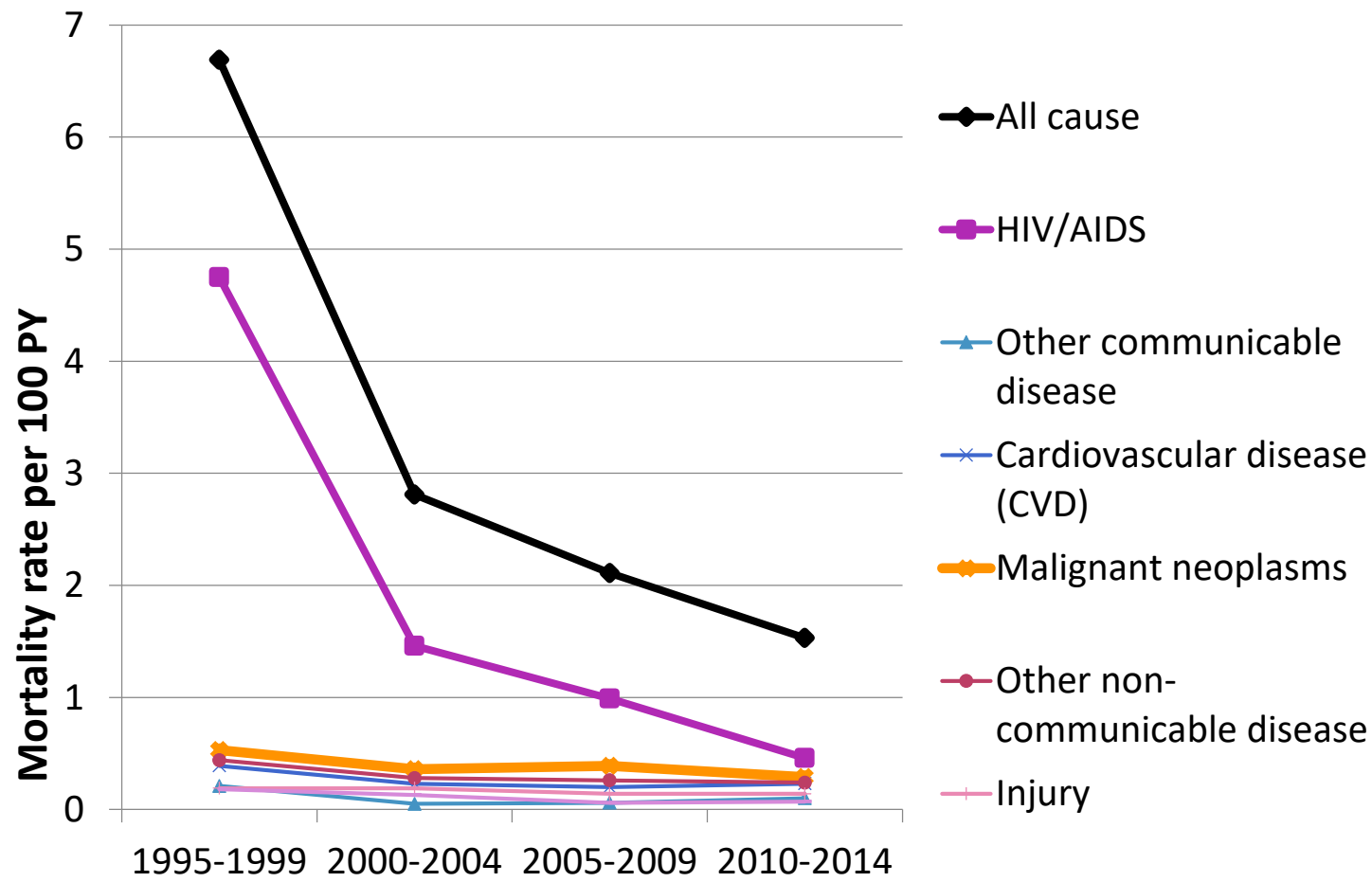
HPV vaccination

Screening with Digital Anal Rectal Exam (DARE)

Screening with cytology, HPV, and other biomarkers

Cancer burden
among people living
with HIV in Ontario

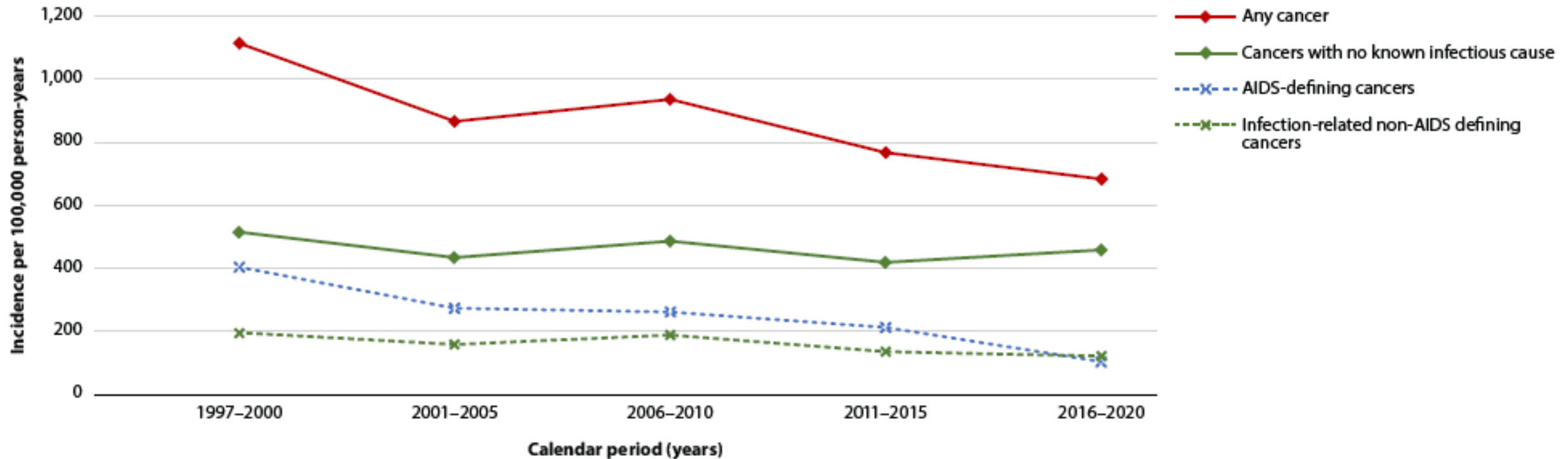
With declines in HIV-AIDS-related mortality among people living with HIV, **malignant neoplasms** have become an increasingly important leading cause of death in Ontario



Burchell et al. Cause-specific mortality among HIV-infected people in Ontario, 1995-2014: a population-based retrospective cohort study. *CMAJ Open* 2019; 7(1):E1-7.

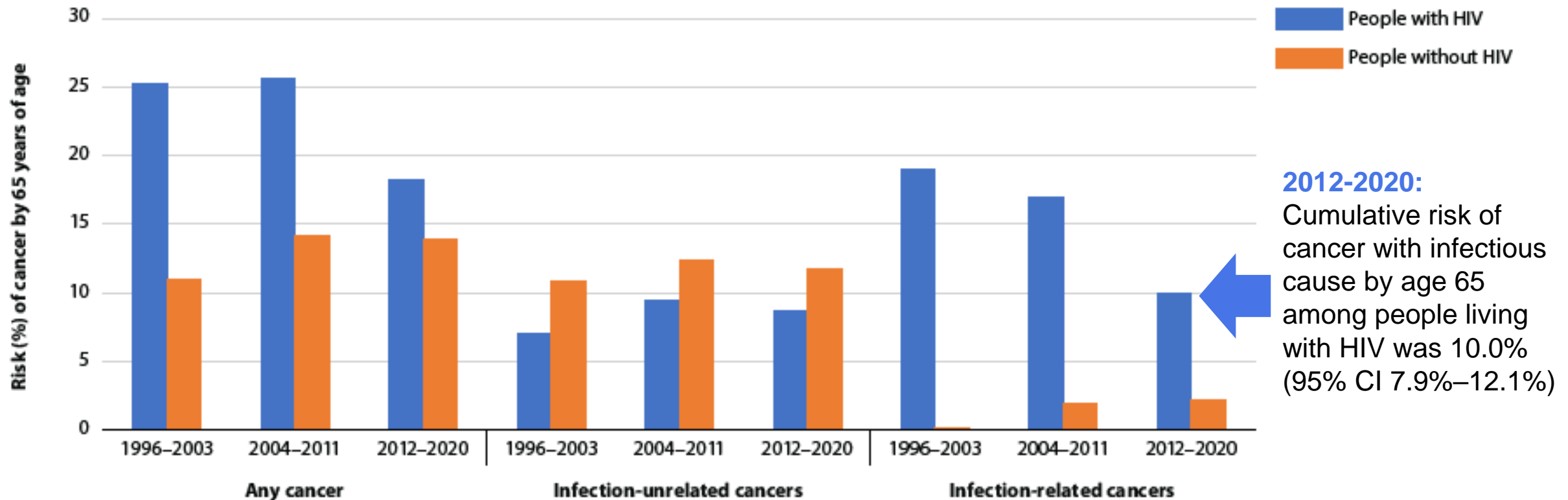
In Ontario, infection-related cancers have declined among people living with HIV, largely driven by declines in AIDS-defining cancers Kaposi sarcoma, non-Hodgkin lymphoma, and invasive cervical cancer

Age-standardized incidence rate (per 100,000 person-years) of first primary cancers among people living with HIV



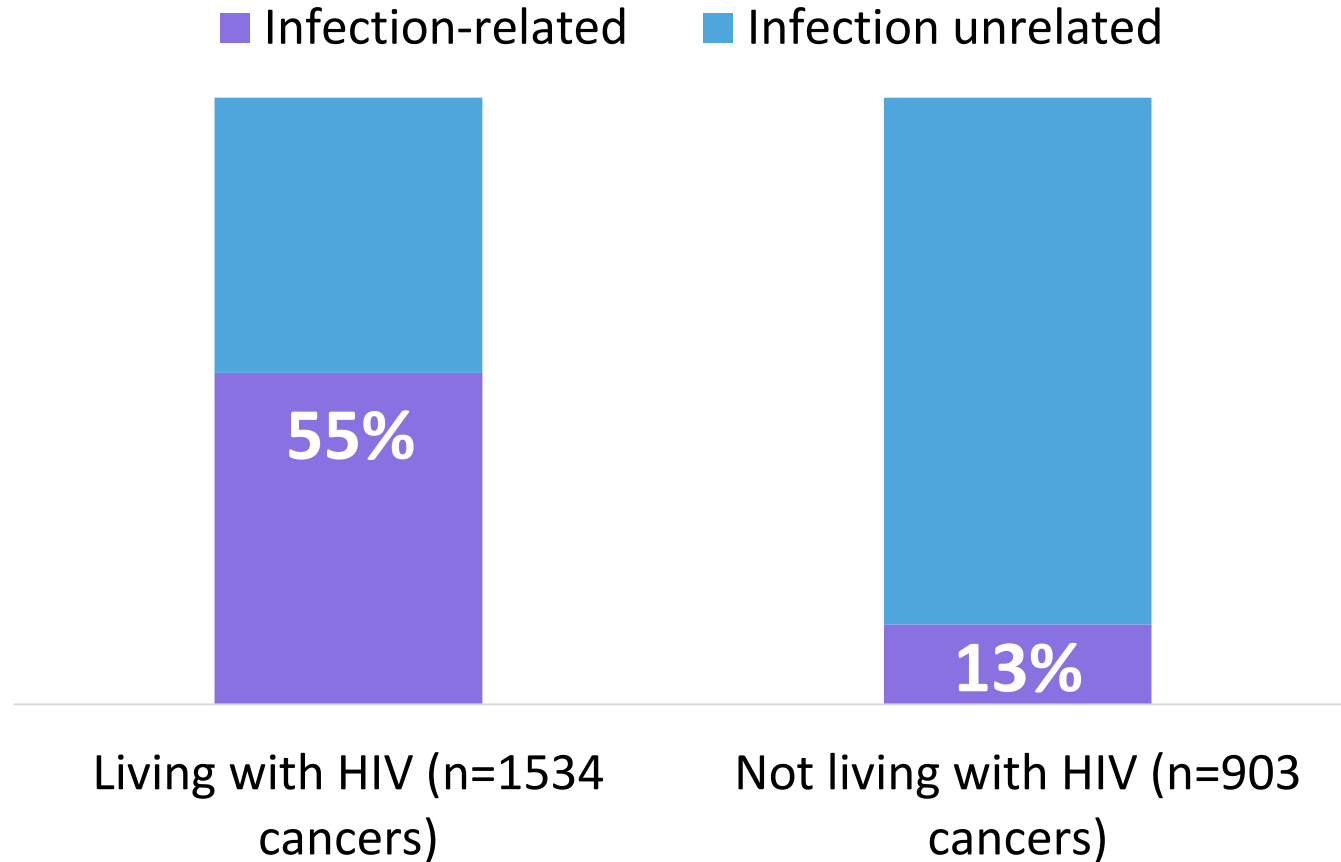
Nicolau, ..., Burchell. The burden of cancer among people living with HIV in Ontario, Canada, 1997-2020: a retrospective population-based cohort study using administrative health data. *CMAJ Open* 2022.

Cumulative incidence risk (%) of cancer by 65 years of age for people living with and without HIV, by calendar period



Nicolau, ..., Burchell. Trends in infection-related and infection-unrelated cancer incidence among people with and without HIV infection in Ontario, Canada, 1996–2020: a population-based matched cohort study using health administrative data. *CMAJ Open* 2023; *in press*.

Distribution of incident first primary cancers diagnosed from a matched cohort study of people with and without HIV infection, 1996-2020



Top 5 cancers among males living with HIV

- Non-Hodgkin lymphoma
- Kaposi sarcoma
- Prostate
- Anus
- Lung

Top 5 cancers among females living with HIV

- Breast
- Non-Hodgkin lymphoma
- Lung
- Genital tract (uterus, ovary, cervix)
- Thyroid

Nicolau, ..., Burchell. *CMAJ Open* 2022.

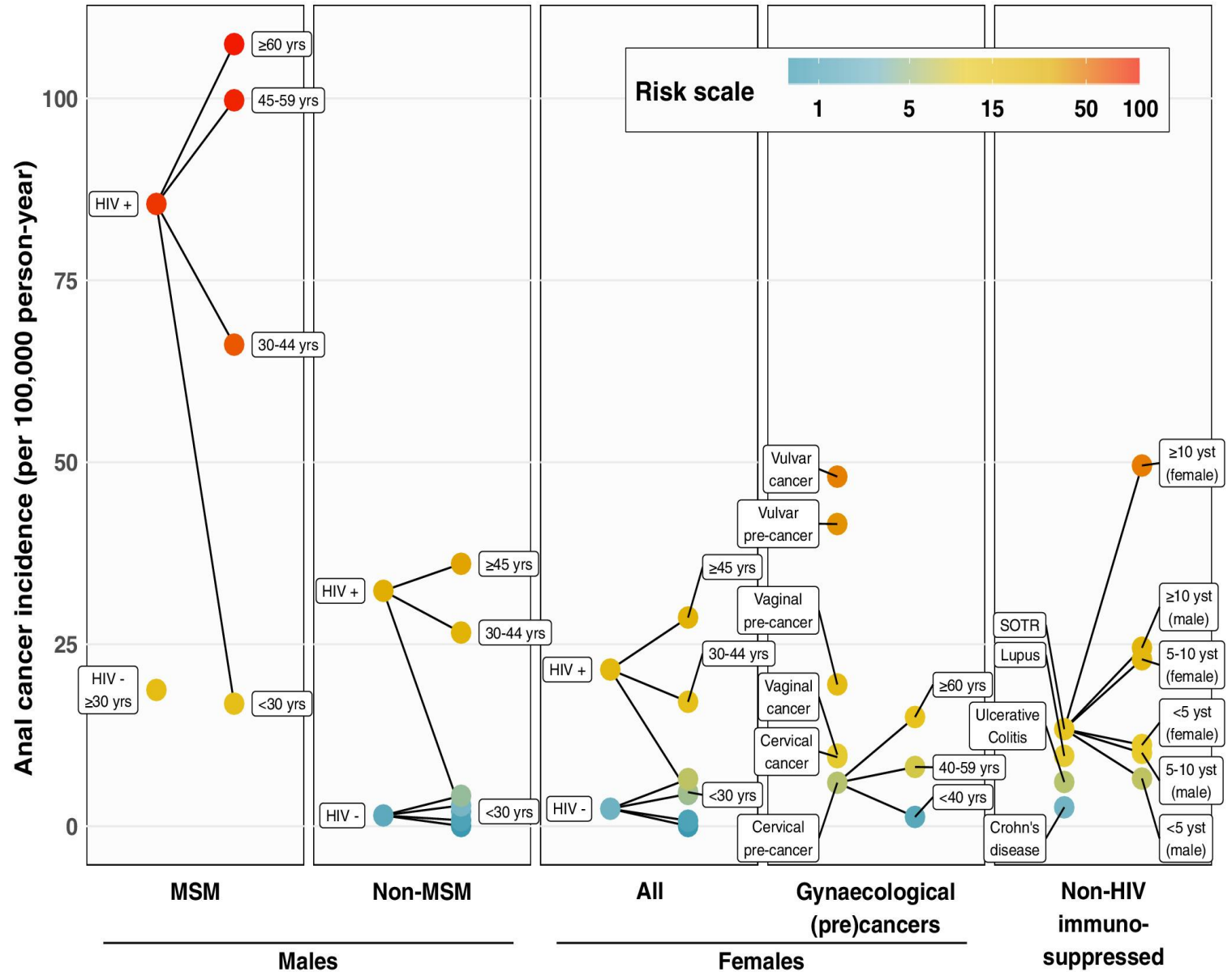
Nicolau, ..., Burchell. *CMAJ Open* 2023; *in press*.

Anal cancer risk and
knowledge among
people living with HIV

Anal cancer risk is higher among people with a compromised immune status, including people living with HIV

Clifford et al.

Int J Cancer 2020; 148(1): 38-47.



People living with HIV older than 30 years, women with history of genital (pre)cancer, solid transplant recipients

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%)



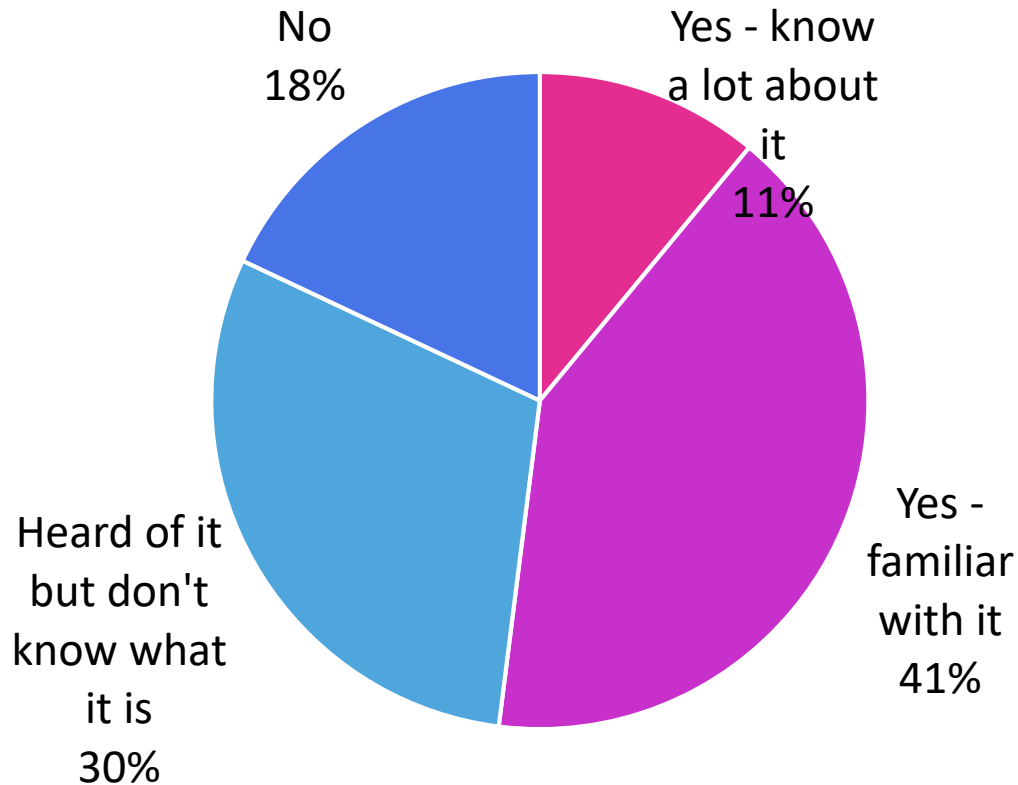
OCS
OHTN COHORT STUDY

- Ontario HIV Treatment Network Cohort Study (OCS) follows people living with HIV attending HIV care clinics across Ontario
- Volunteer participation
- Questions about HPV knowledge, HPV vaccination, cancer screening, and beliefs about screening
- **1677 men living with HIV** interviewed from April 2016 to June 2017
- **619 women living with HIV** interviewed from July 2017 to January 2020

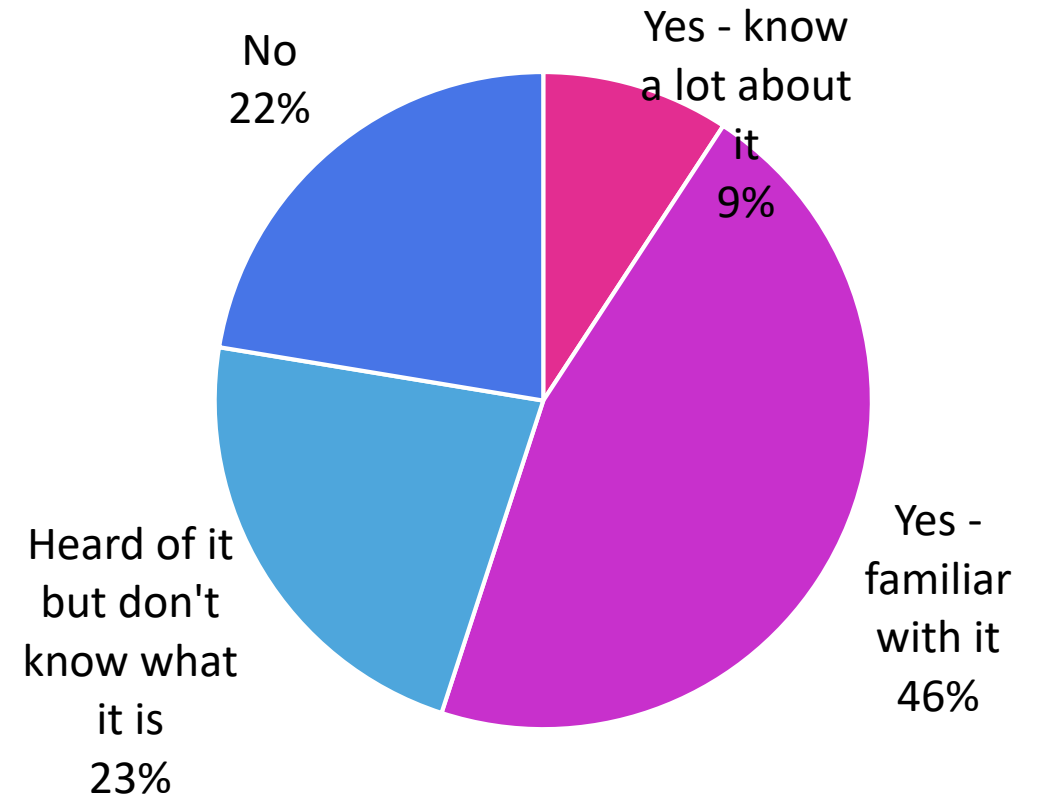


Have you heard of the human papillomavirus or “HPV”?

Men living with HIV



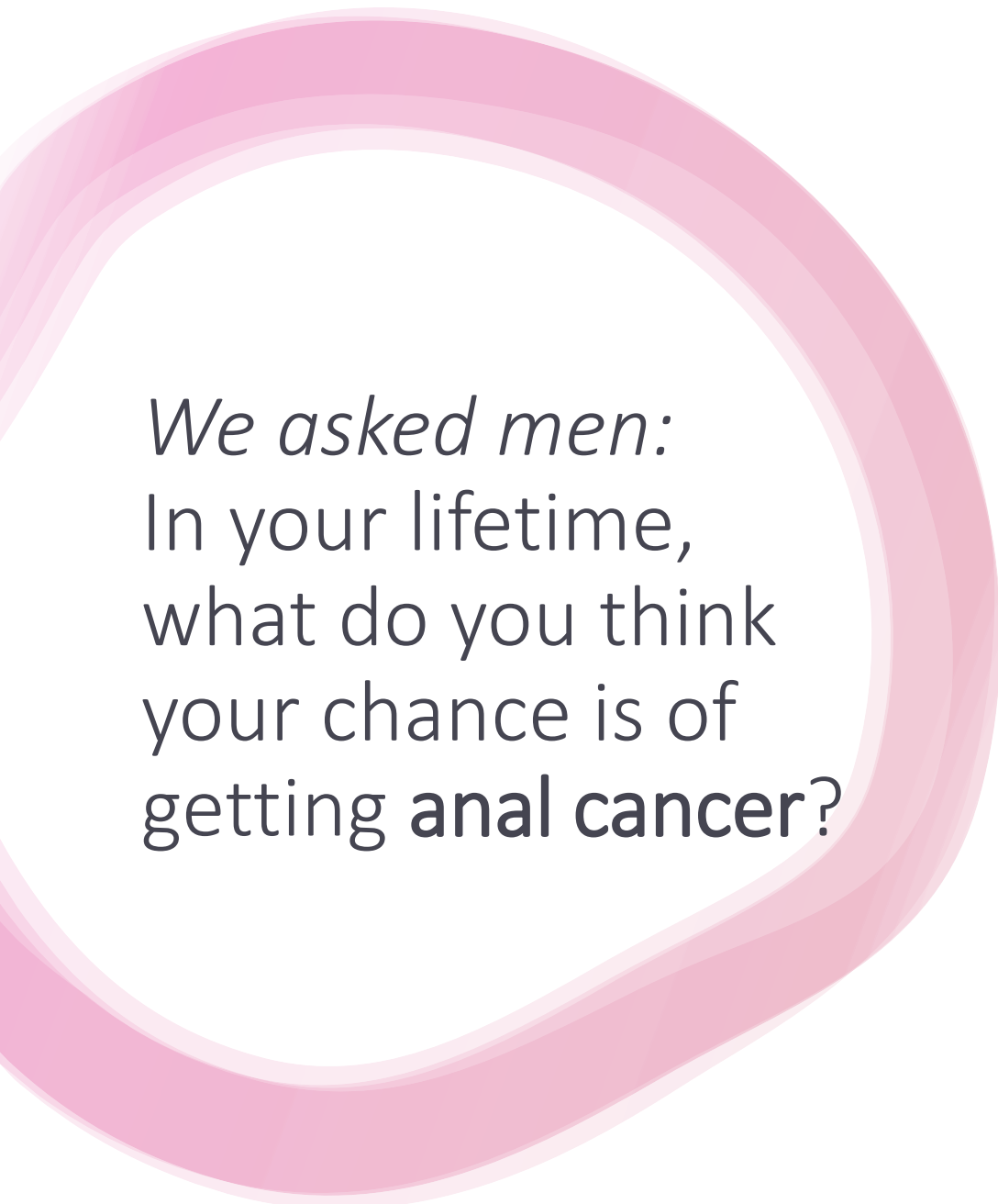
Women living with HIV



Knowledge gaps

- 47% of men and 45% of women did not know that **smoking** increases the chance that HPV infections will progress to cancer
- 18% of men and 22% of women did not know that **living with HIV** increases the chance that HPV infections will progress to cancer

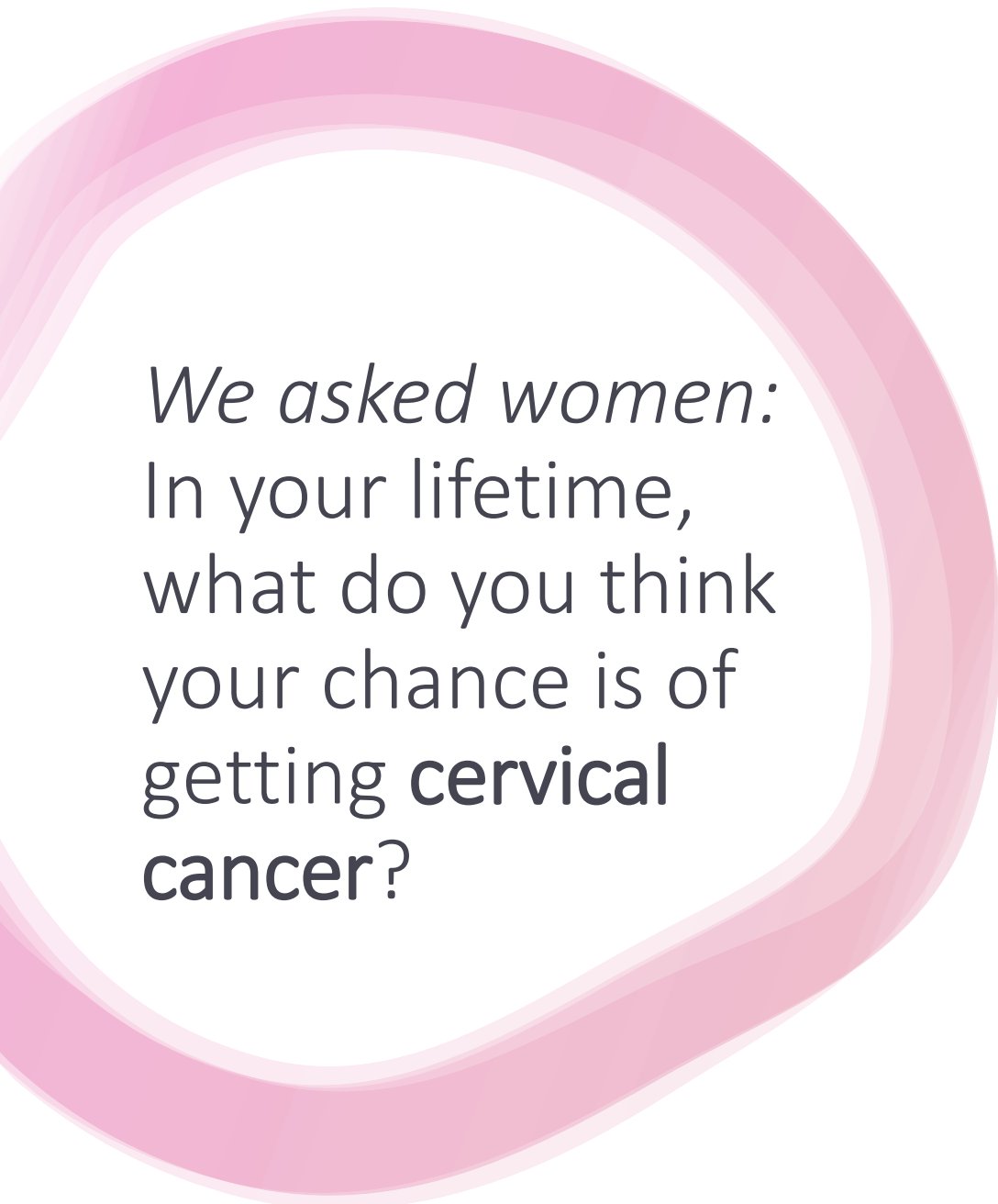




We asked men:
In your lifetime,
what do you think
your chance is of
getting **anal cancer?**

**49% of men said they
had a low chance**

**22% felt they had no
chance**



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

**19% of women didn't
know their risk**

**35% felt they had no
chance**

Vaccination to prevent
HPV infection and anal
cancer

Clinical guidelines for HPV vaccination among people living with HIV: Canada

- “3-dose schedule of the HPV vaccine ... recommended for individuals who are immunocompromised and immunocompetent HIV-infected individuals”
- Immunogenic but seroconversion rates and anti-HPV titres can be lower compared to historical HIV-negative controls, particularly if low CD4 cell count or high viral load

Safe and well tolerated

No evidence of deleterious effects on CD4 cell count or viral load

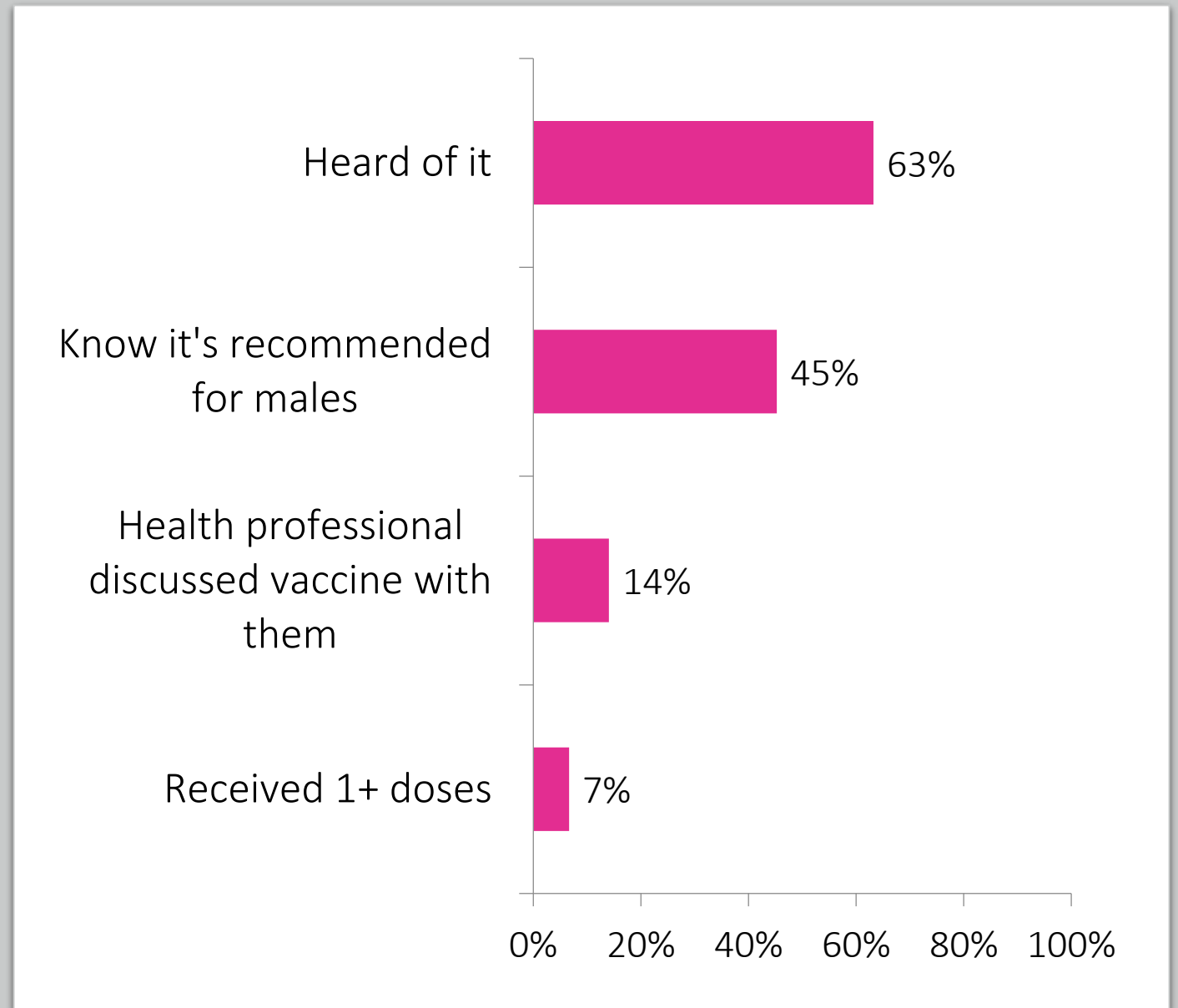
An Advisory Committee Review National Advisory Committee on Immunization (NACI)

NACI Literature Review for HPV Immunization of Immunocompromised Populations

PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH

Experience with HPV vaccine among men living with HIV

Grewal, ..., Burchell. Low human papillomavirus (HPV) vaccine uptake among men living with human immunodeficiency virus (HIV): Cross-sectional findings from a clinical cohort. *Prev Med* 2021.



Only **13.2%** of women received at least 1 dose of HPV vaccine

Of those vaccinated...



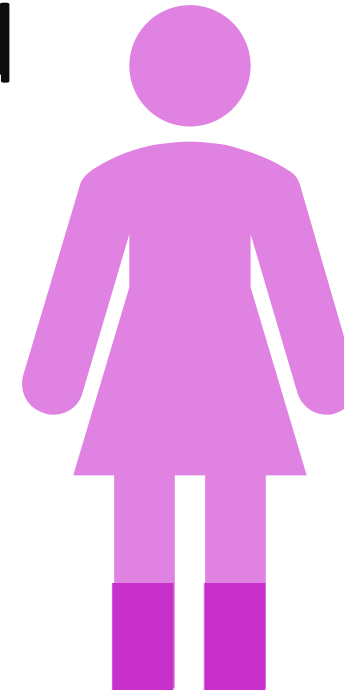
12% received 1 dose



23% received 2 doses



65% received all 3 recommended doses



13.2%

Characteristics associated with having received HPV vaccine (1+ dose)

Men living with HIV

- Younger age
- Identify as gay
- White / non-racialized
- Higher income, education
- Employment
- Extended health insurance coverage
- Recently sexually active, multiple partners with more partners
- Nadir CD4 count >500 cells/mm

Grewal, ..., Burchell. *Prev Med* 2021.

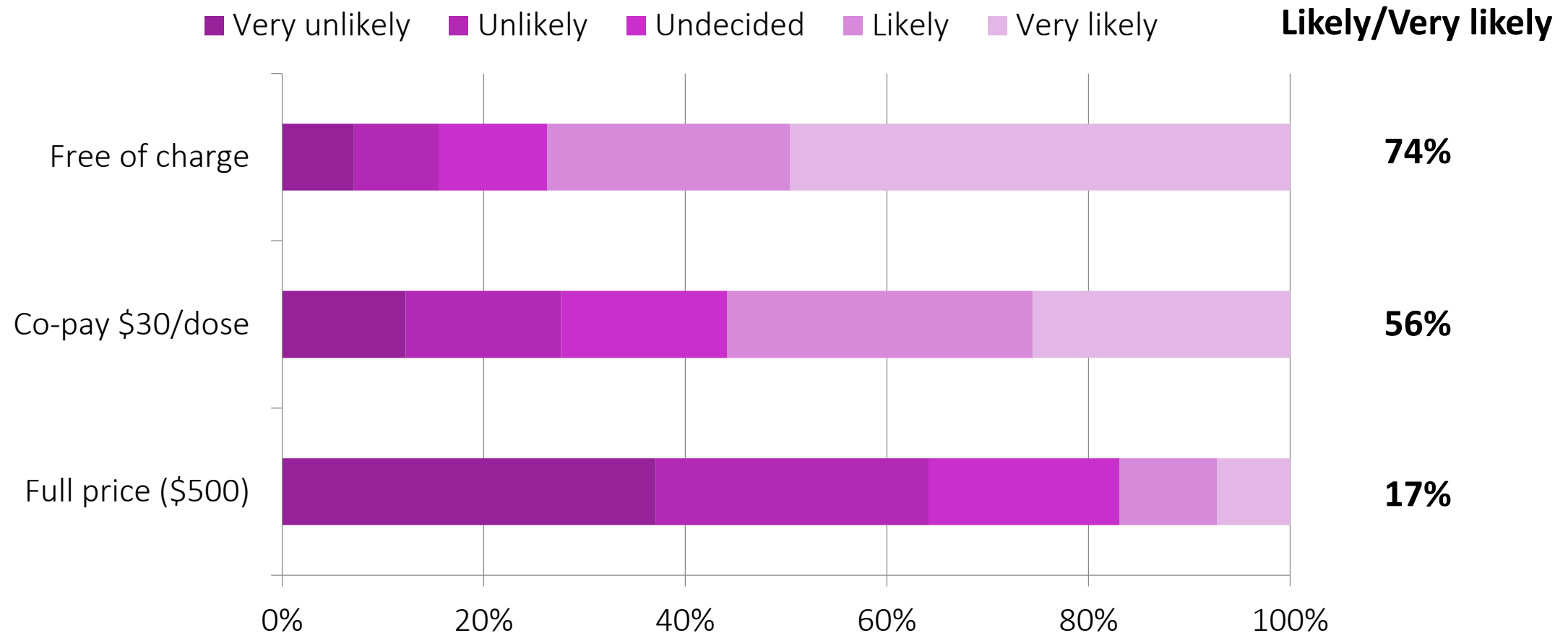
Women living with HIV

- Younger age
- University education
- Employment
- Married or common-law
- Living with children
- Immigrating to Canada >5 years ago
- Non-smoker
- In HIV care for longer

Chambers, ..., Burchell. *Prev Med* 2022.

We asked men:

Think about what you might do in the next year. Would you get the HPV vaccine if it were...

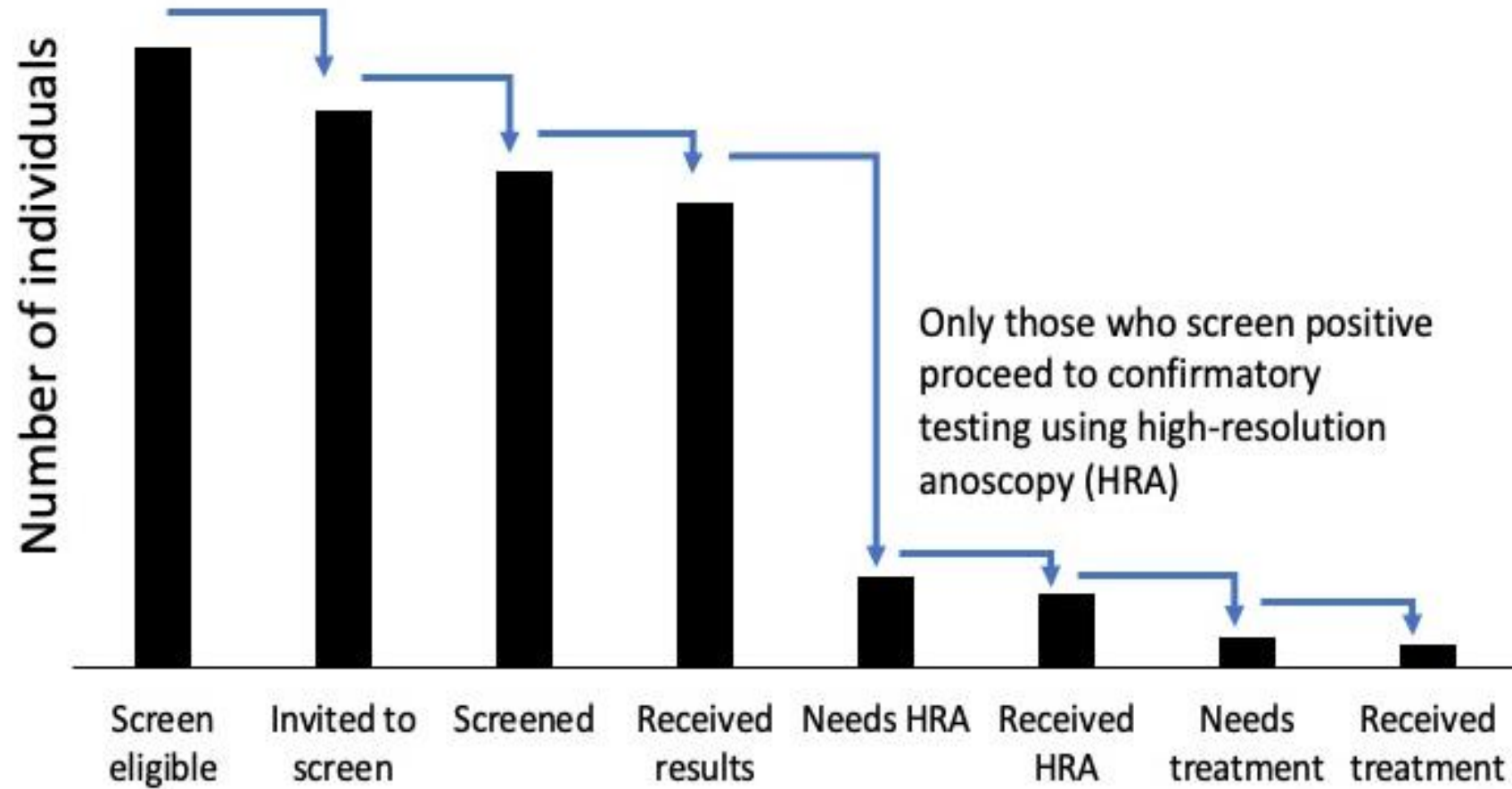


What do these findings tell us about about HPV vaccination for people living with HIV?

- HPV vaccine uptake remains low among people living with HIV despite regular engagement in care and immunization guideline recommendations
- Ways to improve uptake include clinician education and advocating for low/no cost HPV vaccine for people living with HIV

Screening to
prevent anal cancer
progression

Anal screening cascade



International Anal Neoplasia Society Guidelines for the Practice of Digital Anal Rectal Examination

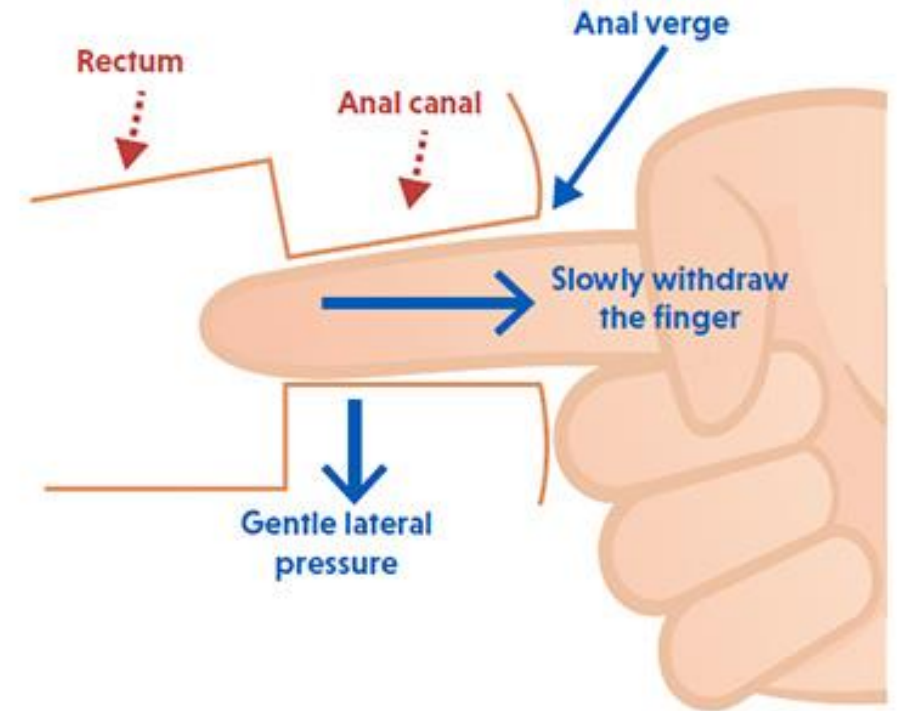
Hillman, Richard John MD; Berry-Lawhorn, J. Michael MD; Ong, Jason J. PhD; Cuming, Tamzin MD; Nathan, Mayura MD; Goldstone, Stephen MD; Richel, Olivier MD, PhD; Barrosso, Luis F. MD; Darragh, Teresa M. MD; Law, Carmella MD; Bouchard, Céline MD; Stier, Elizabeth A. MD; Palefsky, Joel M. MD; Jay, Naomi PhD

Author Information

Journal of Lower Genital Tract Disease 23(2):p 138-146, April 2019. | DOI:

- **Screening for early stage cancer**
- 80% five year-survival of anal cancers diagnosed at <2cm
- 45-65% five year survival rate when cancers are >2cm at diagnosis
- When done properly, DARE can detect cancers ≥ 0.3 cm
- **IANS recommends an annual DARE for people living with HIV**

Figure 1
How to perform a digital anal rectal examination (DARE)



Hillman. www.HPVWorld.com, 161

IS YOUR BUTT GETTING ENOUGH ATTENTION?



**50% OF HIV+ MEN HAVE
PRECANCEROUS ANAL CELLS
AND ARE SYMPTOM- FREE.**

WE NEED HIV+ VOLUNTEERS OF ALL
GENDERS WHO ARE 35+ TO TAKE PART IN A
NATIONAL ANAL CANCER PREVENTION STUDY.

VISIT THE WEBSITE ANCHORSTUDY.ORG
OR CALL 1-800-555-5555



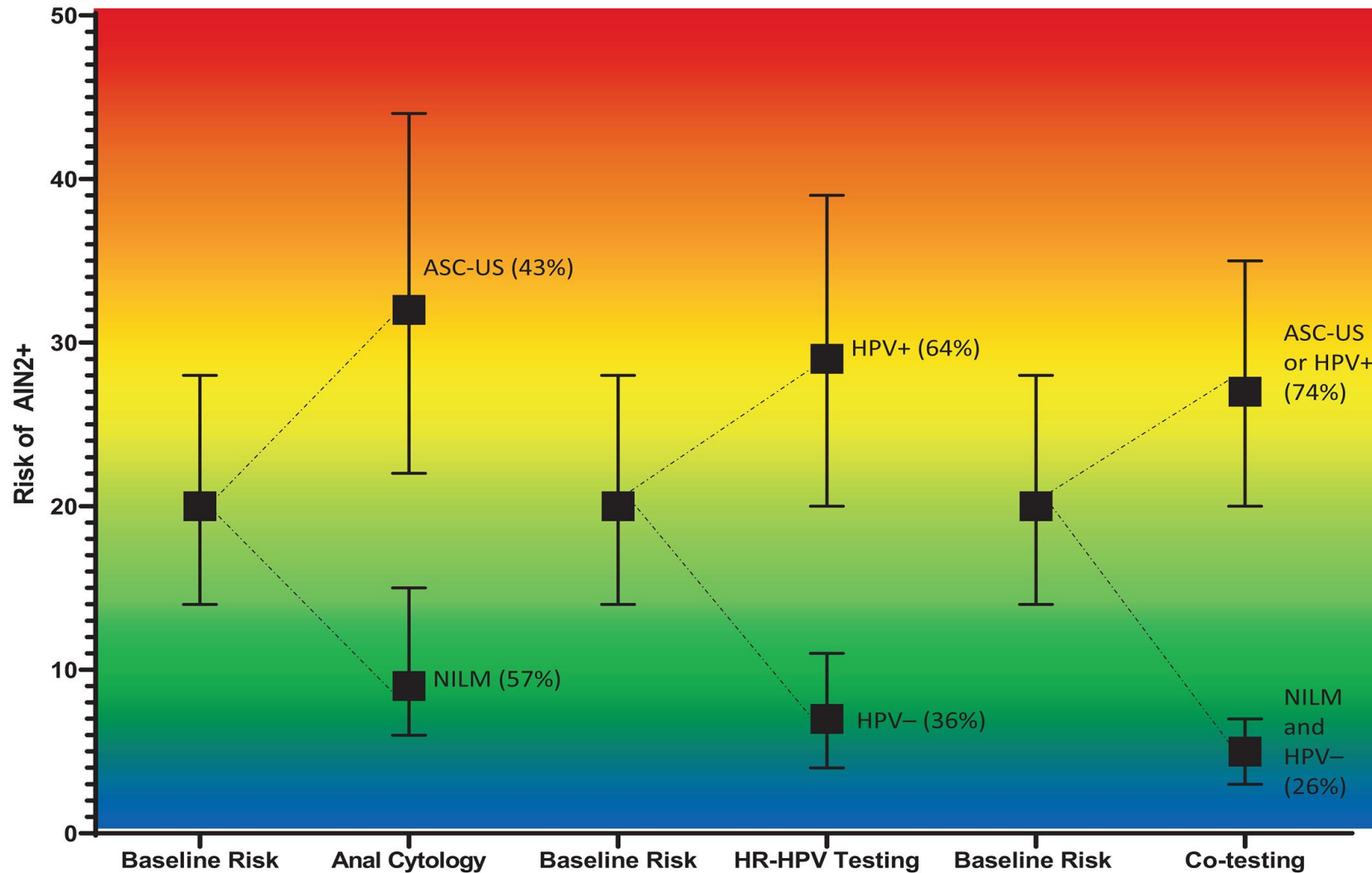
Screening for anal precancer

- Treatment of precancerous lesions in the anus reduced the risk of progression to anal cancer by 57%
- ANCHOR Trial included 4,446 people living with HIV (all genders) aged 35 and older in the United States who had a diagnosis of a high-grade anal precancer followed for ~2 years
- 9 cases of invasive anal cancer in the treatment group
- 21 cases of invasive anal cancer in the “active monitoring” group
- Trial stopped after interim analysis and treatment offered to all in active monitoring arm

New guidelines for anal PRECANCER screening anticipated from the International Anal Neoplasia Society (IANS)

- Age-based recommendations for ALL living with HIV regardless of gender or sexual orientation
 - Age 35 years and older for men who have sex with men and trans women
 - Age 45 years and older for all others living with HIV
 - In Ontario, we estimate that this could be as many as 17,000 people
- What screening test(s) to use?
- When to refer for high resolution anoscopy?
- *Will depend on local resource availability*

Absolute risk for anal intraepithelial neoplasia (AIN) 2+ for cytology, HPV testing, or co-testing



AIN2+, anal intraepithelial neoplasia grade 2 or worse

ASC-US+, atypical squamous cells of undetermined significance or worse

NILM, negative for intraepithelial neoplasia or malignancy

Clarke et al. A systematic review and meta-analysis of cytology and HPV-related biomarkers for anal cancer screening among different risk groups. *Int J Cancer* 2022.



Predicting and Evaluating Anal Cancer in HIV with novel biomarkers The PEACH Study

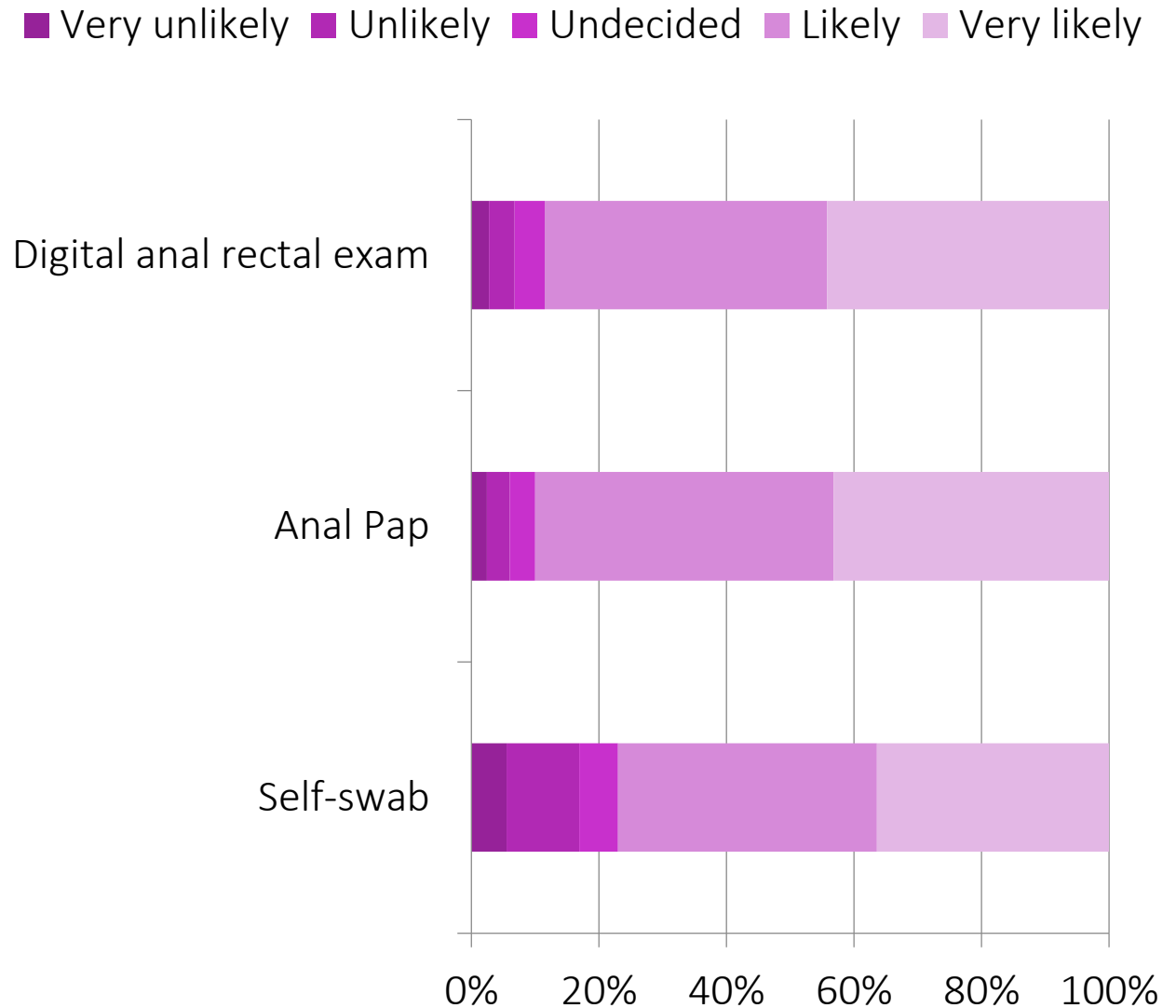
- Observational study to recruit 1000 gay, bisexual, and other men who have sex with men, and transgender women living with HIV in Vancouver and Toronto
- Will explore other biomarkers beyond cytology and HPV DNA testing
- **Aim:** to better predict who is at higher risk of having or developing high grade precancerous anal lesions
 - Cytology
 - HPV DNA testing
 - E6/E7 mRNA expression
 - p16-Ki67 dual stain (cytology)
 - HPV viral load

PEACH Team

Troy Grennan	Jennifer Gillis	Ronita Nath
Ann Burchell	Daniel Grace	Gina Ogilvie
Irving Salit	Ramandip Grewal	Ron Rosenes
Joshua Edward	Mark Hull	Darrell Tan
Mark Gaspar	Paul MacPherson	Ed Weiss

Most men living with HIV in Ontario would be willing to have anal cancer screening, if offered in the next year

Gillis, ..., Burchell. Influence of previous experience with and beliefs regarding anal cancer screening on willingness to be screened among men living with HIV. *BMC Public Health* 2022.



Percent "likely" and "very likely" to accept an offer of an anal Pap test in the next year, if offered, among OHTN Cohort Study participants aged 35 and older (Men: 2016-2017; Women: 2018-2020)

	n	Likely	Very Likely
Gender			
Women	485	54%	20%
Men	1476	46%	43%
Men: Age			
35-49 years	431	48%	39%
50-59 years	664	46%	46%
60+ years	381	41%	47%
Women: Age			
35-49 years	248	52%	19%
50-59 years	155	57%	21%
60+ years	82	50%	18%

	n	Likely	Very Likely
Men: Sexual orientation			
Gay	1073	41%	51%
Bisexual	99	56%	30%
Heterosexual	279	56%	24%
Other sexual orientation	14	43%	43%
Women: Sexual orientation			
Heterosexual	446	53%	19%
Lesbian, bisexual, other sexual orientation	38	60%	26%

Percent "likely" and "very likely" to accept an offer of an anal Pap test in the next year, if offered, among OHTN Cohort Study participants aged 35 and older (Men: 2016-2017; Women: 2018-2020)

	n	Likely	Very Likely
Gender			
Women	485	54%	20%
Men	1476	46%	43%
Men: Age			
35-49 years	431	48%	39%
50-59 years	664	46%	46%
60+ years	381	41%	47%
Women: Age			
35-49 years	248	52%	19%
50-59 years	155	57%	21%
60+ years	82	50%	18%

	n	Likely	Very Likely
Men: Race			
White	1062	42%	50%
African/Caribbean/Black	137	58%	25%
Asian	97	49%	33%
Indigenous	57	46%	37%
Latin American	64	53%	31%
Multiracial	49	55%	41%
Women: Race			
White	148	50%	19%
African/Caribbean/Black	254	55%	20%
Other racialized women	57	53%	17%

Other
correlates of
willingness to
have anal
screening
among men
living with HIV

Comfortable discussing anal health with
their family doctor

Positive beliefs about screening (e.g.
confident they can get screened;
disagree that they will feel pain)

Self-perception of higher risk for anal
cancer

What do these findings tell us about about implementation of anal screening for people living with HIV?

- Improving HPV and anal cancer literacy will be important
- Tailored community-led initiatives to facilitate participation in anal screening should address people's understanding of their risk
- Equity focus to determine and dismantle the reasons why racialized persons, heterosexual men, and women may be less likely to engage

Implementation climate among clinicians providing care to people living with HIV?

- **Cautious optimism**

- Facilitators

- Agreement that anal cancer is a significant and urgent health concern for people living with HIV
- Providers observe high rates of HPV-associated disease in this population, including anal cancer deaths among their patients
- Most are generally supportive regarding implementation of anal screening

Gaspar et al. Diagnosing uncertainty: The challenges of implementing medical screening programs for minority sub-populations in Canada. *Soc Sci Med* 2020.

Higashi et al. Anal cancer screening among women with HIV: provider experiences and system-level challenges. *AIDS Care* 2022.

Ong et al. Why are we not screening for anal cancer routinely - HIV physicians' perspectives on anal cancer and its screening in HIV-positive men who have sex with men: a qualitative study. *BMC Public Health* 2015.

Implementation climate among clinicians providing care to people living with HIV?

- **Cautious optimism**

- Barriers

- Concerns that there is inadequate health system capacity to accommodate screen test positives for referral to HRA, and treatment if needed
- Existing HRA services are predominantly in Toronto
- Uncertainty regarding interpretation of screening test results for HRA referral decision-making
- Anticipation of negative reactions from patients (e.g., embarrassment, discomfort)

Gaspar et al. Diagnosing uncertainty: The challenges of implementing medical screening programs for minority sub-populations in Canada. *Soc Sci Med* 2020.

Higashi et al. Anal cancer screening among women with HIV: provider experiences and system-level challenges. *AIDS Care* 2022.

Ong et al. Why are we not screening for anal cancer routinely - HIV physicians' perspectives on anal cancer and its screening in HIV-positive men who have sex with men: a qualitative study. *BMC Public Health* 2015.

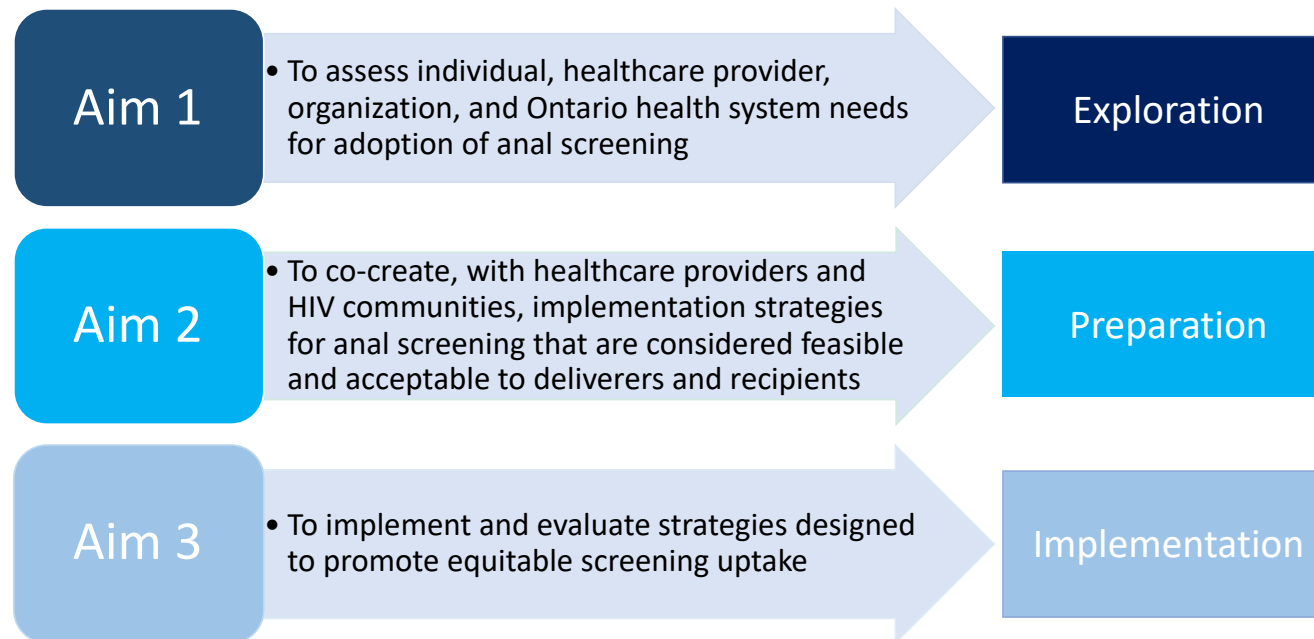
ACCESS Study

(Anal CanCer Equity in Screening Services)

- **Overall goal:** to gather evidence for implementation of equitable anal screening for people living with HIV
- Equity according to age, sex & gender, sexual orientation, race/ethnicity, geography

ACCESS Study Team

Ann Burchell
Troy Grennan
Meghan Walker
Gordon Arbess
Tyler Chesney
Christine Fahim
Daniel Grace
Charlie Guiang
Tae Hart
Aisha Lofters
Paul MacPherson
Devan Nambiar
Mary Ndung'u
Apondi Odhaimbo
Ron Rosenes
Irving Salit
Michael Silverman
Kevin Woodward



First Steps: Needs assessment

- Focus groups and one-on-one interviews with people living with HIV
- One-on-one interviews with clinicians who provide care to people living with HIV
- Discussion guides informed by Theoretical Domains Framework (TDF) and Consolidated Framework for Implementation Research (CFIR)



Aim 1

- To assess individual, healthcare provider, organization, and Ontario health system needs for adoption of anal screening

Exploration

More resources

Free webinars on anal cancer prevention

International Anal Neoplasia Society

www.iansoc.org

International Papillomavirus Society

<https://ipvsoc.org/>

Resources for people diagnosed with anal cancer

<https://www.analcancerfoundation.org/>



**IANS Scientific Meeting 2023
PUERTO RICO**

REGISTER NOW!

Registration is open
for IANS next
Scientific Meeting in
San Juan,
Puerto Rico.

This is an *in-person*
meeting!

November 10-12, 2023
See you there!

Ann.Burchell@unityhealth.to