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**CATIE Webinar Series (Part 1)**  
**Gay Men's Health & HIV Prevention  
in Canada**

***The HPV Question: HPV and Gay, Bisexual,  
Two-Spirit and other MSM in Canada***

Date: February 7, 2012, 2-3:30pm EST

# Webinar Agenda

- Review of the webinar technology
- Project Background
- **HPV in Men**, presented by Dr. Irv Salit
- Questions & Discussion

# TIPS

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# Project Background

- **March 2010:** Pan-Canadian Deliberative Dialogue titled "New Directions in Gay Men's Health & HIV Prevention in Canada"
- **2011:** Initiation of a one-year Gay Men's Sexual Health Project
  - **Formation of a National Advisory Group (NAG)**
- **January 2012:** National Webinar commences



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# *The HPV Question: HPV and Gay, Bisexual, Two-Spirit and other MSM in Canada*

English Only: Tuesday, February 7<sup>th</sup>, 2012, 2pm EST

With an HPV vaccine approved for boys and men, what do we need to know about gay/bi/MSM men, HIV and HPV? How does HPV affect gay/bi/MSM men, and who should be getting the HPV vaccine?

Join us for a presentation from Dr. Irving Salit, Associate Professor of Medicine at the University of Toronto. Dr. Salit is a specialist in Internal Medicine and Infectious Diseases and the Director of the Immunodeficiency (HIV) Clinic at the Toronto General Hospital. His research interests include the Human Papillomavirus (HPV) and screening tests for HPV-associated anal cancer.

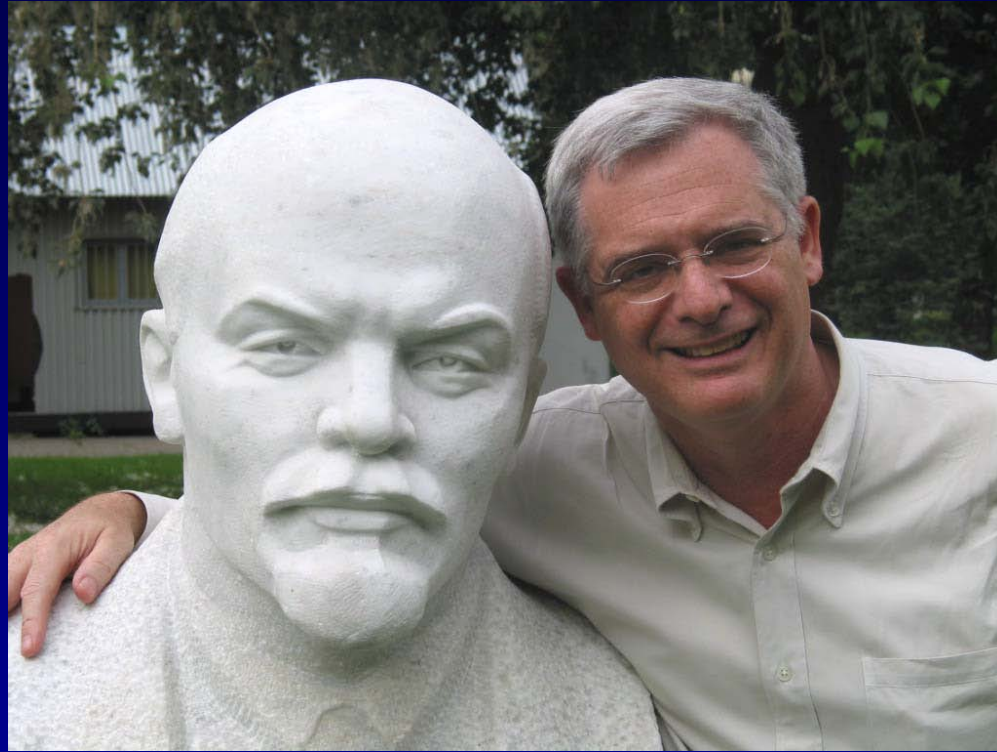




# HPV IN MEN

February 2012





**IRV SALIT**

**Director  
Immunodeficiency Clinic  
Toronto General Hospital**

**Professor of Medicine  
University of Toronto**

# OBJECTIVES

1. The epidemiology of HPV infection
2. Transmission of HPV
3. The range of HPV diseases
4. Controlling HPV
5. The role of HPV vaccination

**HPV**

# HPV

- **DNA virus**
- **Cannot grow in tissue culture**
- **Have to detect in other ways**

# HPV TYPES

- **>100 types: 40 infect genital tract**
- **Genital warts: types 6 and 11**
- **Cancers: types 16 and 18 (31 and 45)**

# HPV INFECTION

Normal Tissues



Low grade lesions (AIN1)



High grade lesions (AIN 2/3)



Cancer

} = Dysplasia

# HPV PREVALENCE

- **Cervix: 5-25% (but 70-90% in women with multiple partners)**
- **Penis: 20-45%**
- **Anus: 40-75% (women with multiple partners); 60-95% (MSM)**
- **Oro-pharynx: 0.5-20%**

# EPIDEMIOLOGY



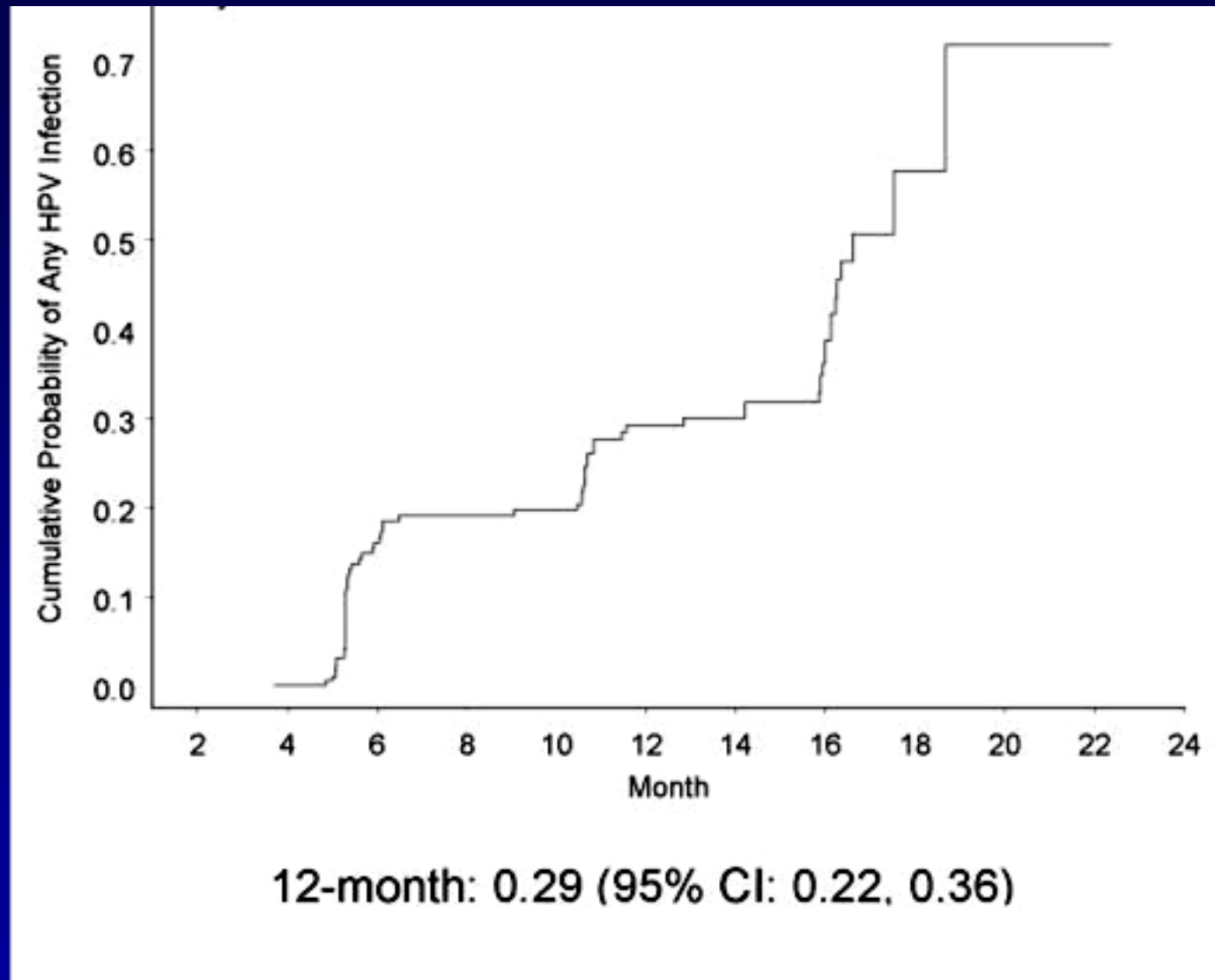
# HPV - MALE GENITAL INFECTIONS

- Penile shaft - 52%
- Scrotum - 40%
- Glans/Corona - 32%
- Urine - 10%
- Semen - 6%

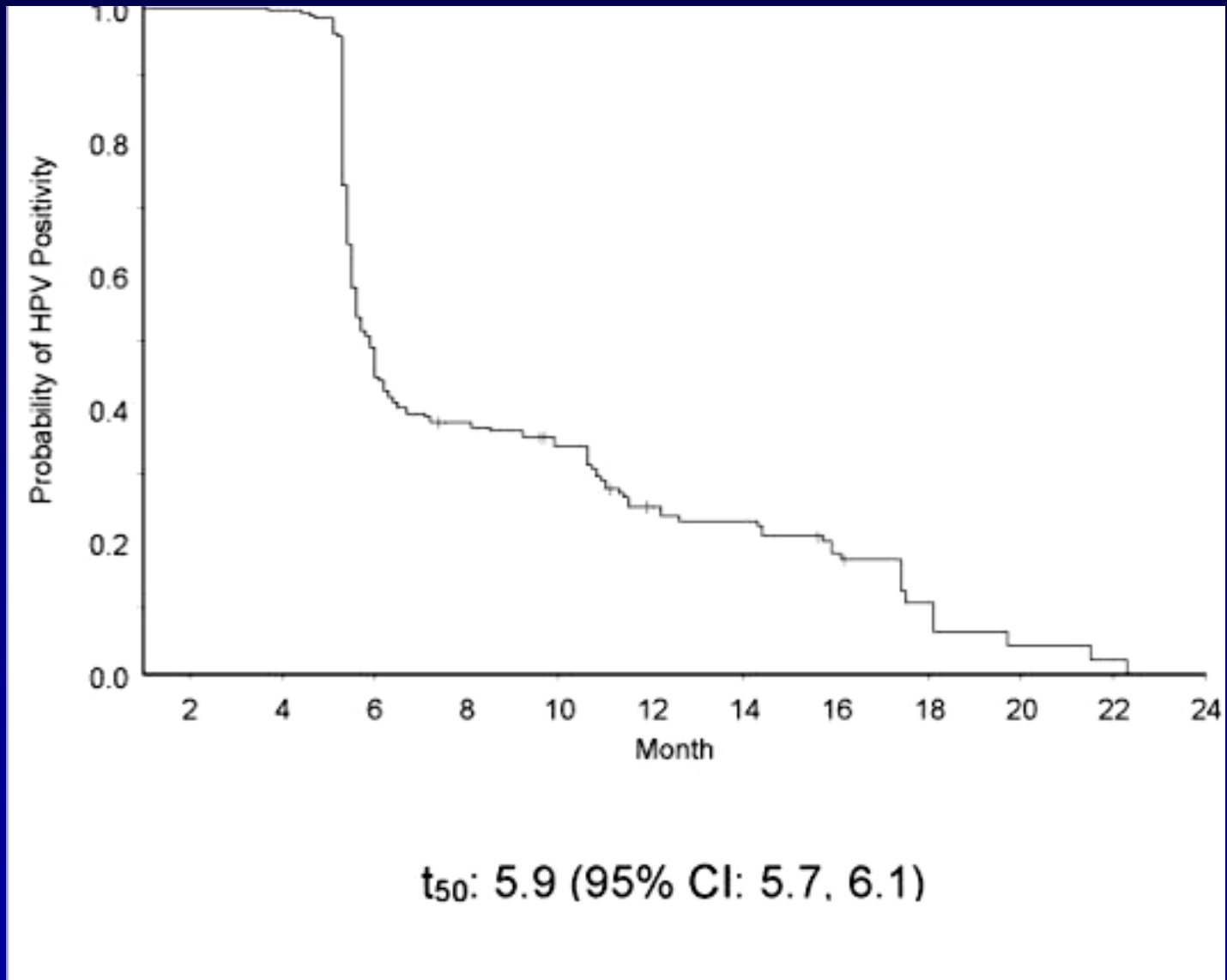
# ANAL HPV AND GAY MEN

	HIV+	HIV-
HPV+ (PCR)	93%	61%
Multiple HPV	73%	23%
HPV-16	35%	9%
Hi risk HPV	80%	29%

# HPV ACQUISITION IN MEN



# HPV CLEARANCE in MEN



# HPV and HIV

- **Increased risk of getting HIV if HPV on penis<sup>1</sup>**
- **Increased risk of getting HIV if HPV in anus in MSM<sup>2</sup>**

1. Smith. The Journal of Infectious Diseases 2010; 201(11):1677–1685  
2. Chin-Hong .AIDS 2009, 23:1135–1142

# HPV TRANSMISSION

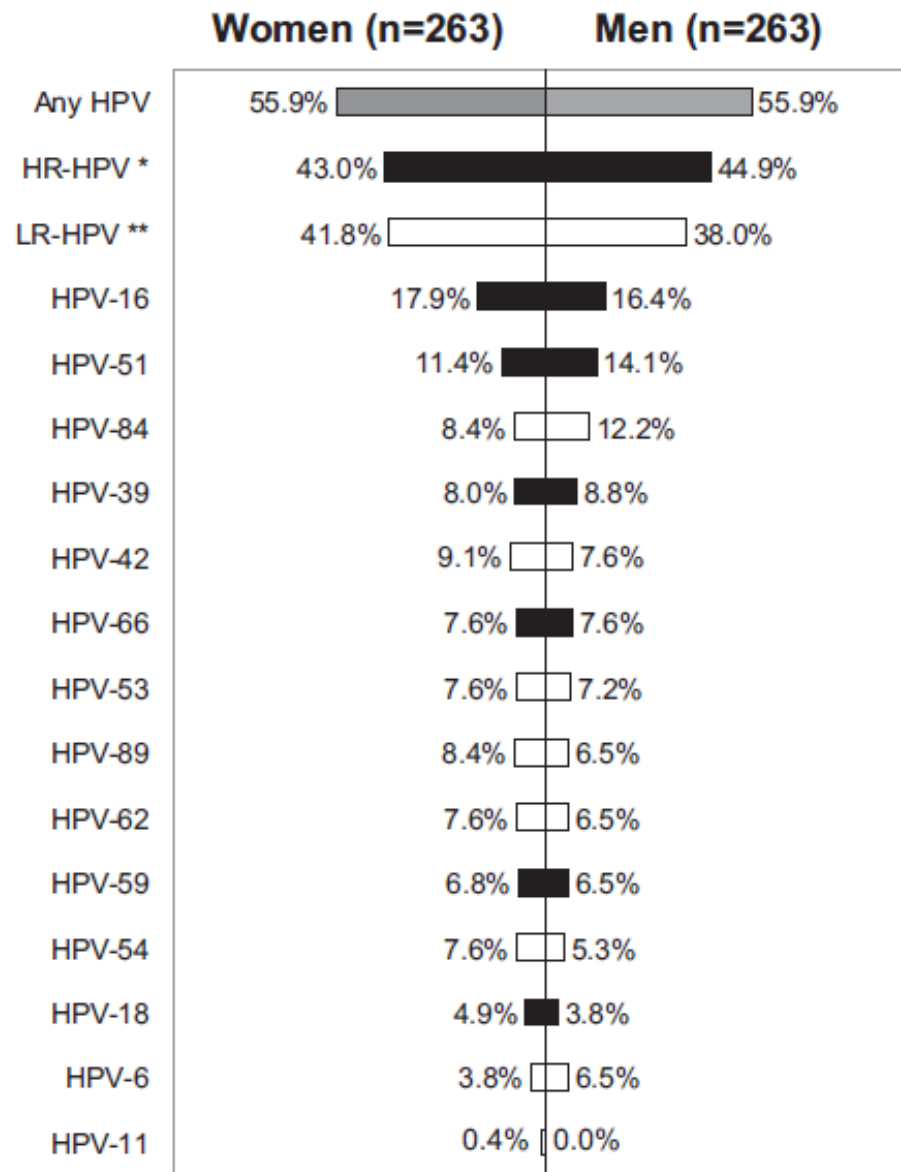


Figure 1. HPV prevalence at enrolment among women and men in a new sexual relationship, HITCH Cohort Study, 2005–2008. \*HR-HPV indicates high-risk onco-

# CIRCUMCISION

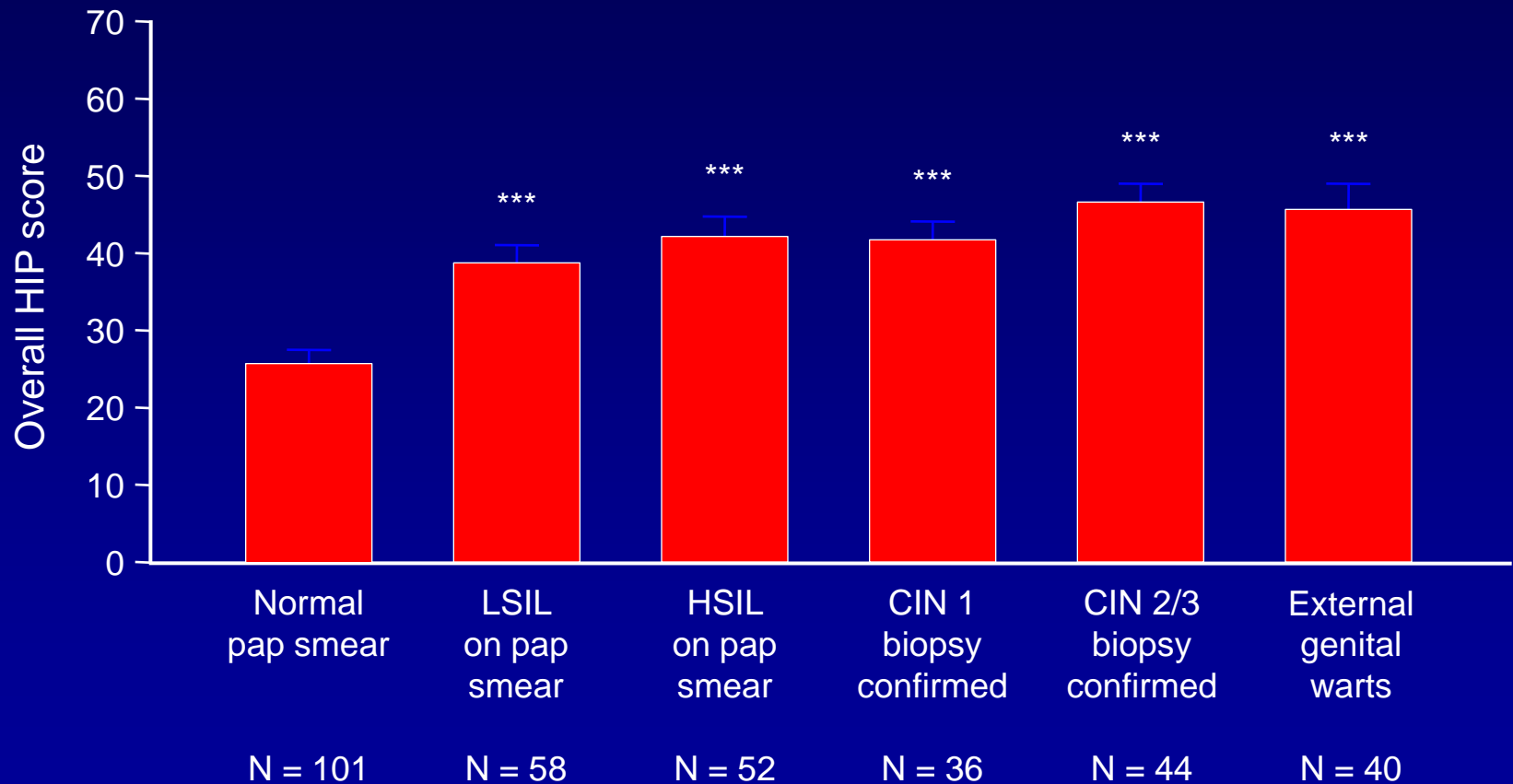
- **Penile HPV less common if circumcised**
- **Women whose male partners were circumcised had a lower risk of cervical cancer**
- **Probably circumcision reduces risk of anal cancer in MSM partner (?)**



# HPV- RELATED DISEASES

**WARTS**

# The Psychosocial Burden of HPV-related Disease: Overall HIP (HPV Impact Profile) Scores by Study Group



# HPV and CANCERS

**Table 1: Average annual number of cases and age-standardized incidence of HPV-associated cancers among persons aged 15 years and older in Canada (1997-2006) and estimated attributable proportion due to HPV.**

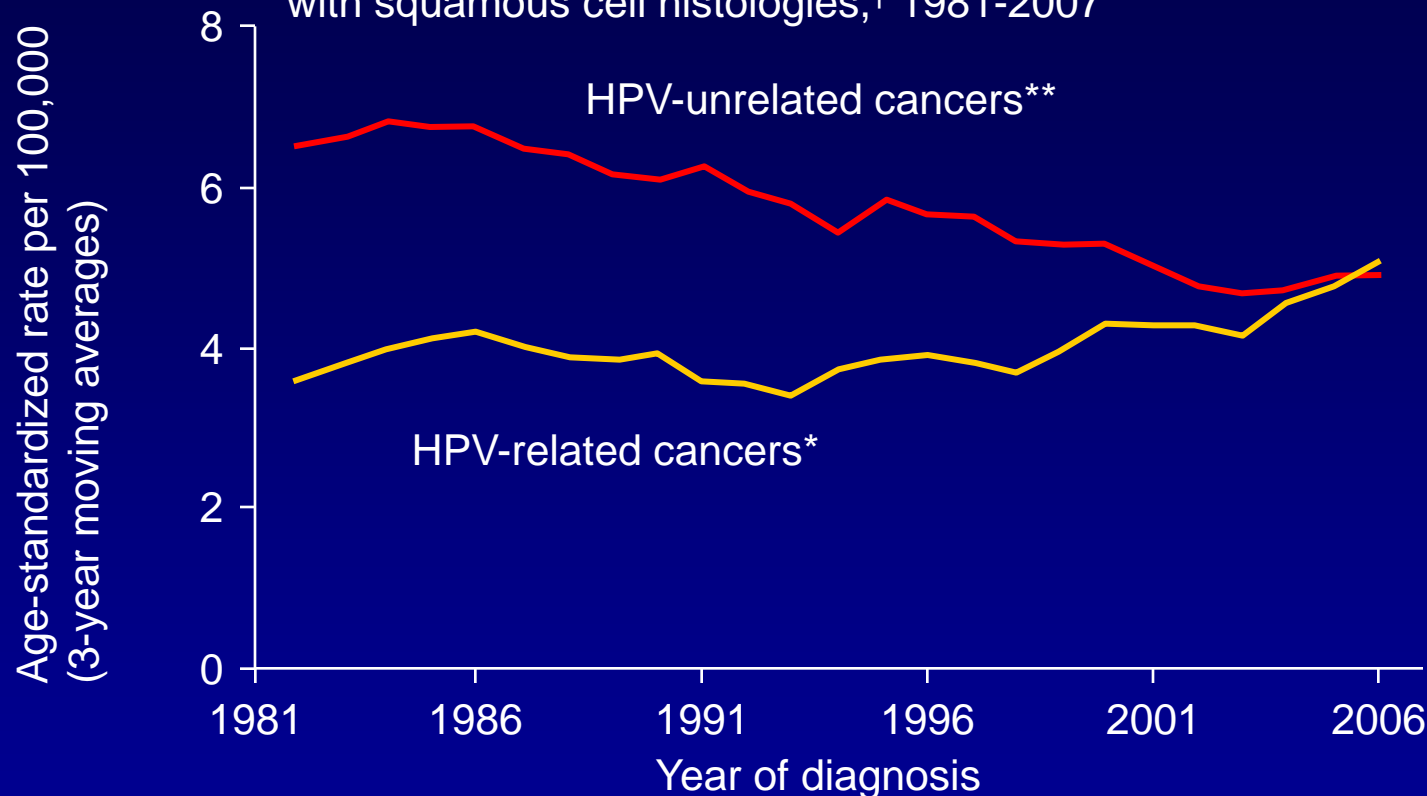
Sex	Anatomical site*	Average annual incidence (per 100 000) <sup>(43)</sup>	Average annual number of cases	Estimated attributable proportion (%) <sup>(38, 41, 42)</sup>	
				Any HPV type	HPV types 16 and 18 (% of all HPV types)
Males	Penis	1.0	127.4	50	63
	Anus	1.6	208.2	90	92
	Oral cavity	6.5	853.1	25	89
	Oropharynx	0.64	84.3	35	89
Females	Cervix	10.1	1356.8	100	70
	Vagina and vulva	4.2	651.8	40	80
	Anus	1.7	267.0	90	92
	Oral cavity	3.3	501.2	25	89
	Oropharynx	0.18	27.2	35	89

# ORO-PHARYNX



# Oral cancer in adult men - Ontario

New cases of oral cancer in Ontario adult men aged 20+ with squamous cell histologies,† 1981-2007



Source: Cancer Care Ontario (Ontario Cancer Registry, 2010)

\* HPV-related cancers: squamous cell carcinomas of the base of tongue, lingual tonsil, tonsil oropharynx, and Waldeyer ring (C019, C024, C090-C109, C142)

\*\* HPV-unrelated cancers: squamous cell carcinomas of the tongue, gum, floor of mouth, palate, other & unspecified parts of the mouth (C020-C023, C025-C069)

† Squamous cell histologies: ICD-O-3 8050-8076, 8078, 8083-8084, 8094

Cancer Care Ontario. Cancer Fact: HPV-related oral cancers increasing among Ontario men. July 2011.

Available at <http://www.cancercare.on.ca/cancerfacts>. Prepared by surveillance staff in Prevention and Cancer Control.

# PENILE CANCER

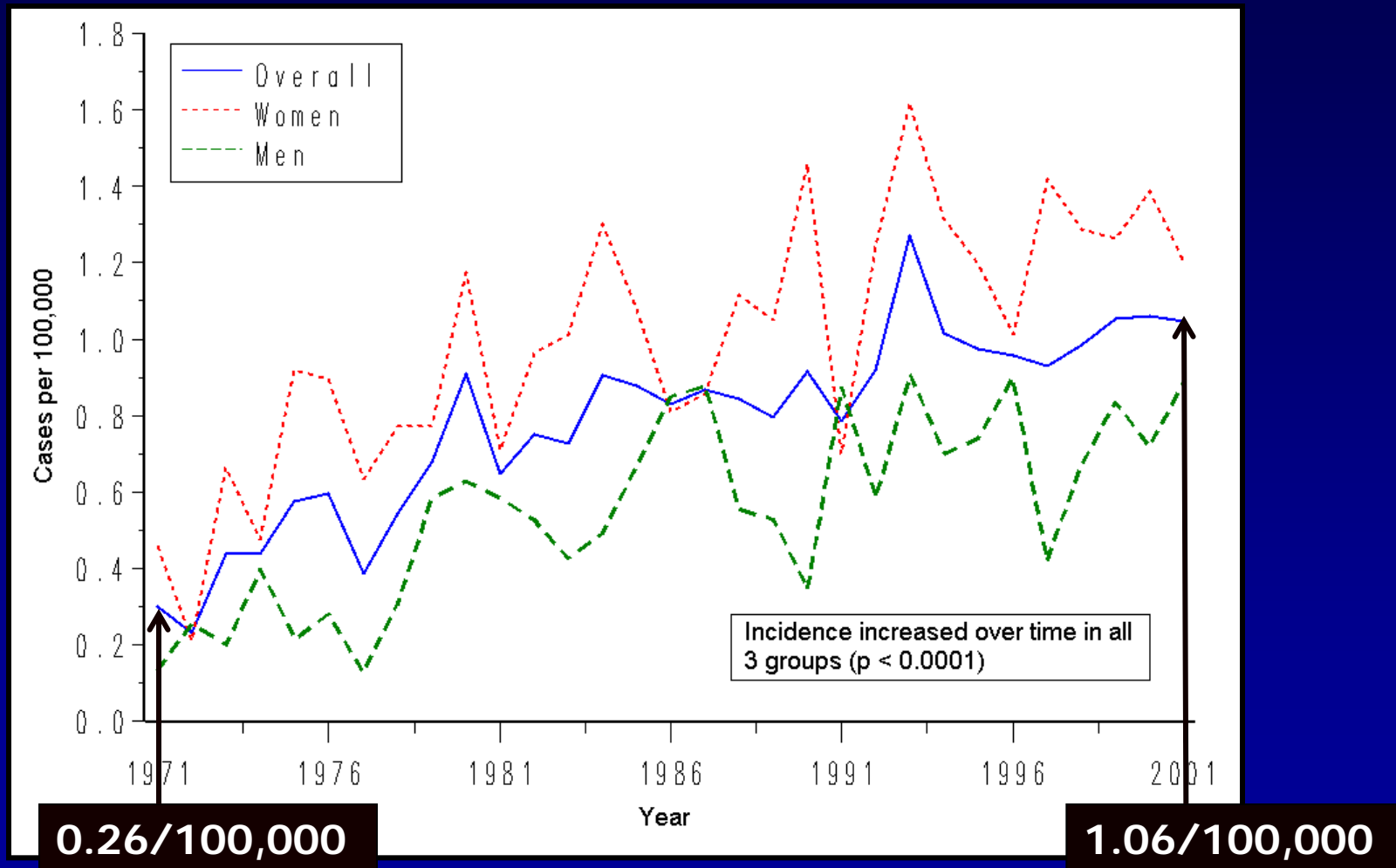


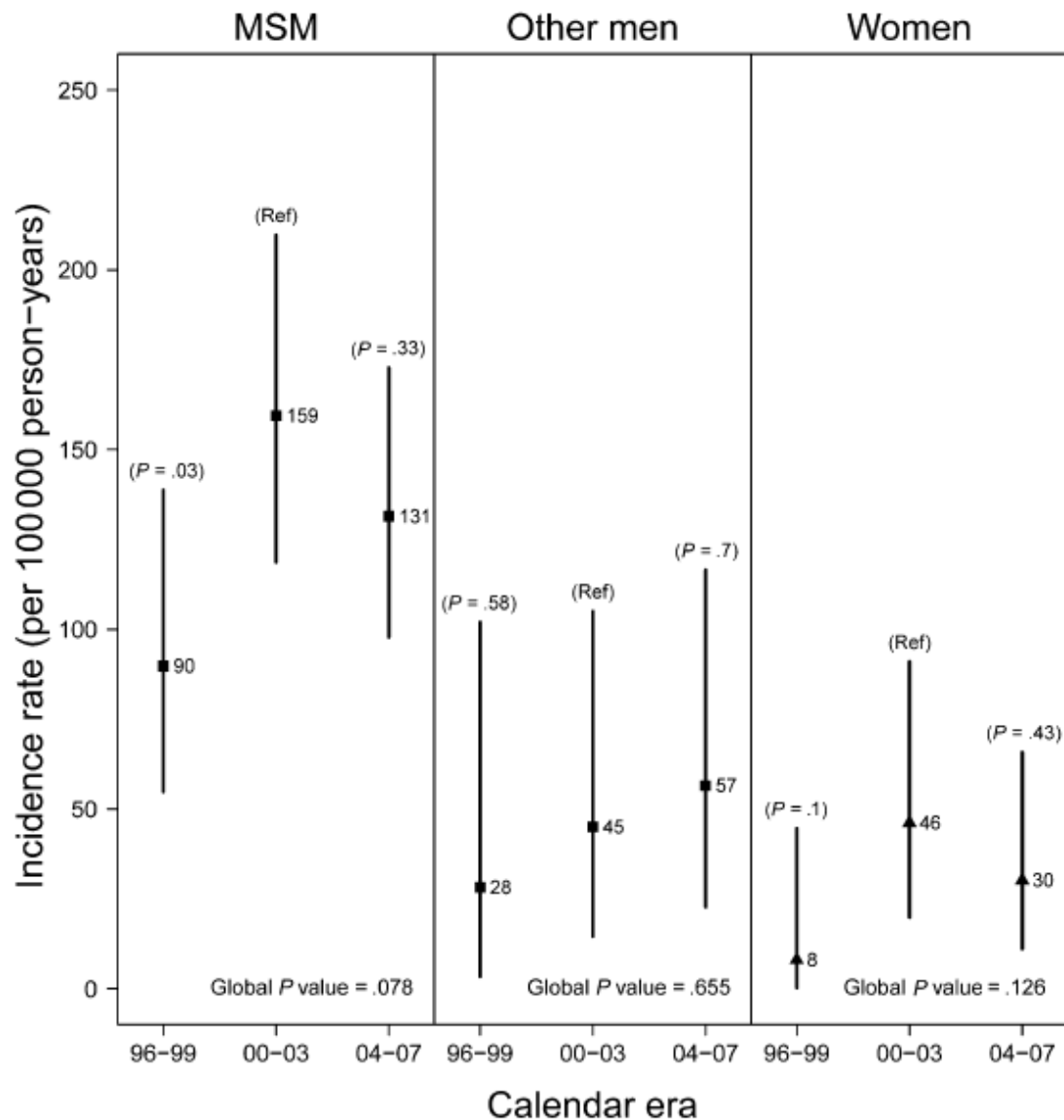




# **ANAL CANCER**

# Age- & Sex-Adjusted Anal Cancer Incidence, 1971-2002





**Figure 2.** Anal cancer incidence rates by calendar era for human immunodeficiency virus infected men who have sex with men (MSM), other men, and women, North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD), years 1996–2007. Vertical lines are 95% confidence intervals. *P* values from the Poisson regression model compare rates by calendar era with 2000–2003 as reference. The global *P* value for comparison of rates across eras is based on the likelihood ratio statistic.

# ANAL CANCER AND MSM

- Anal cancer highly associated with anal sex (OR = 33)<sup>1</sup>
- Anal cancer is up to 163x more common in HIV+ MSM

1. Daling, NEJM 1987

2. Frisch, J NCI 2000

**ABNORMAL IMMUNE STATUS**

**CANCER**

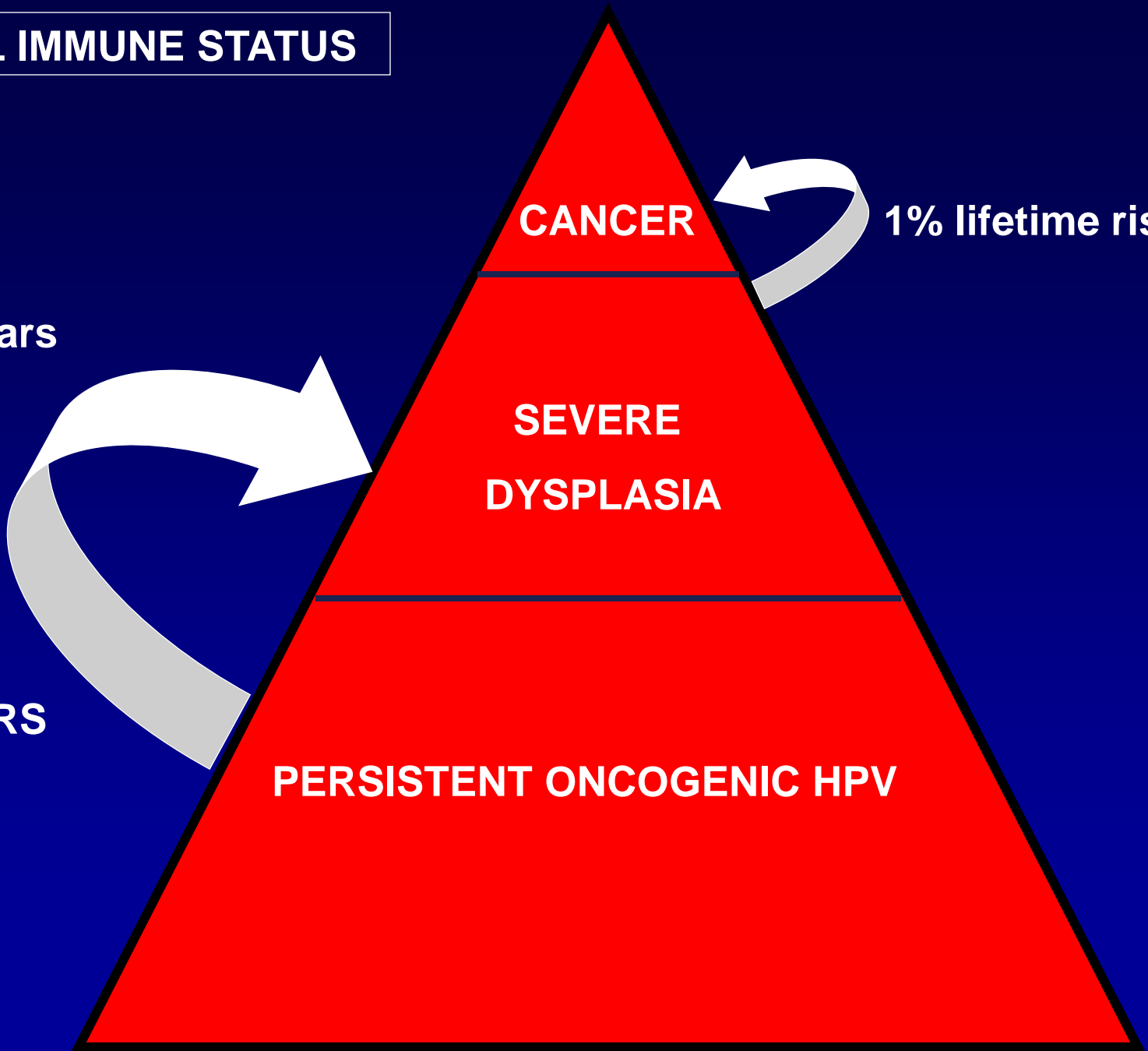
**1% lifetime risk**

**SEVERE  
DYSPLASIA**

**20% at 4 years**

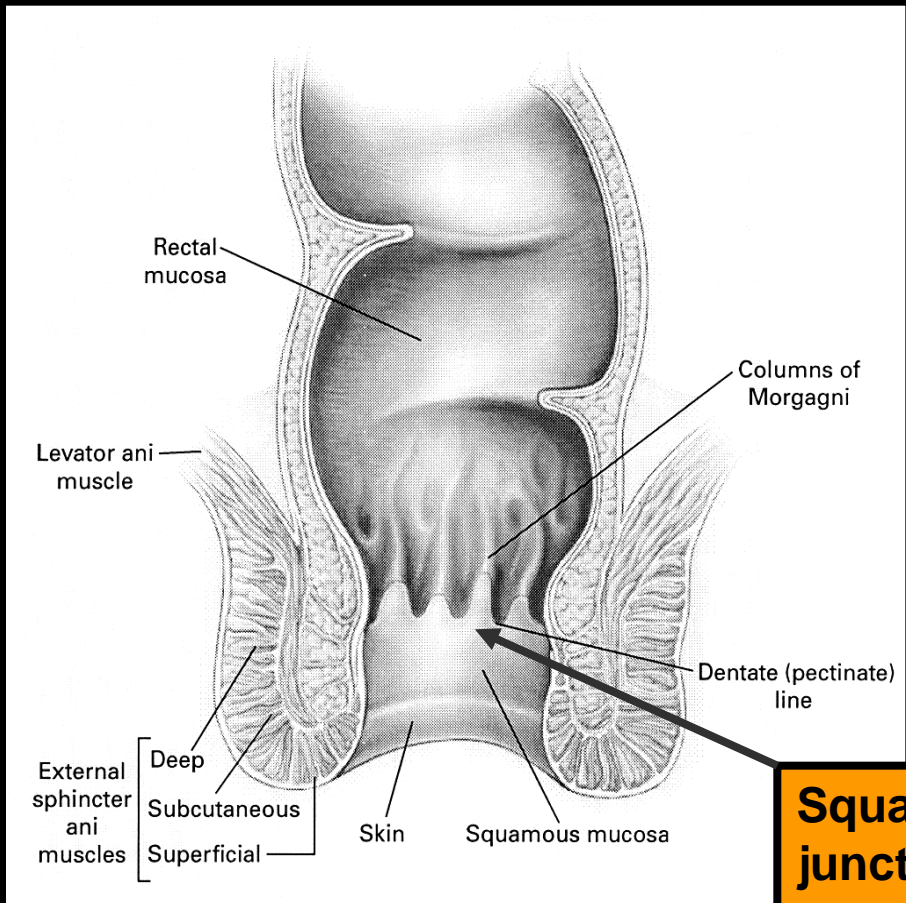
**PERSISTENT ONCOGENIC HPV**

**CO-FACTORS**  
**-HIV**  
**-Smoking**



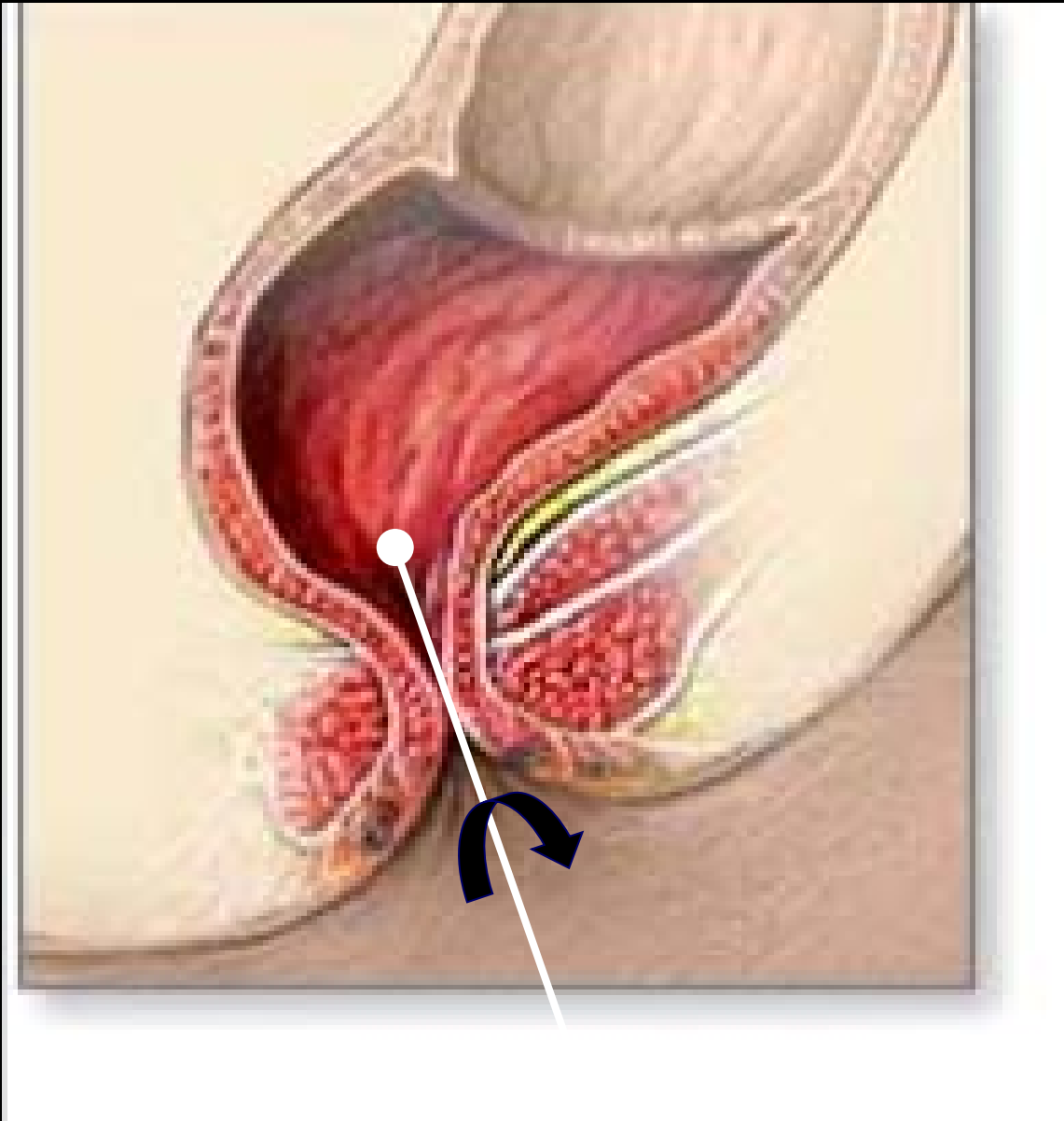
**CAN WE PREVENT ANAL  
CANCER?**

# SCJ: where columnar epithelium of the rectum (endocervix) meets the squamous epithelium of the anus (exocervix)





# ANAL PAP SMEAR



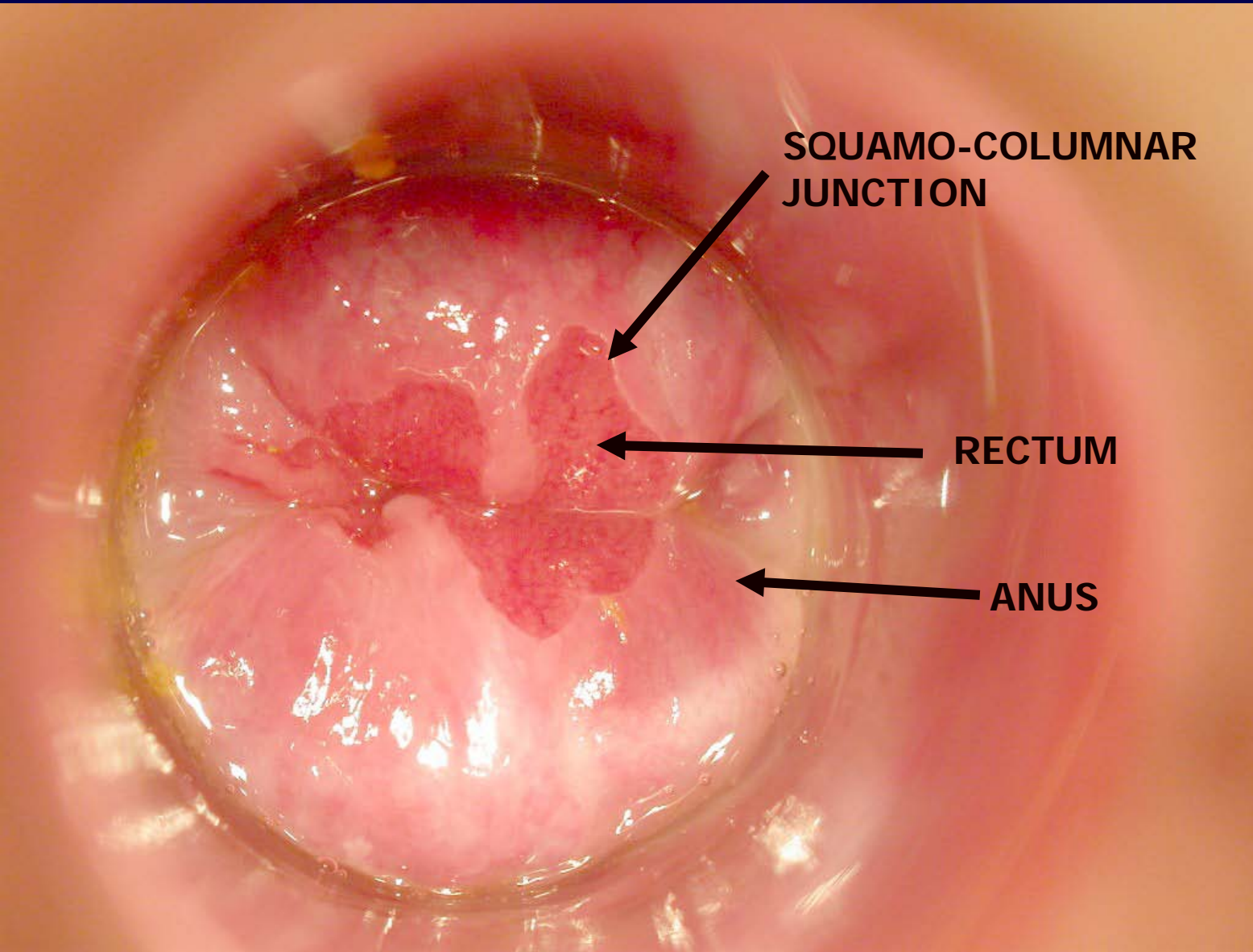


ANAL CYTOLOGY

- 1. Wash the Pap
- 2. Spread the Pap
- 3. Label the slide
- 4. Perform wet mount - report smear back - changed Pap
- 5. Perform Papanicolaou and save
- 6. Review if necessary

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# NORMAL SQUAMO-COLUMNAR JUNCTION



SQUAMO-COLUMNAR  
JUNCTION

RECTUM

ANUS

# TRACE STUDY

- **Screening for anal pre-cancers in HIV+ MSM**
- **Rates of serious pre-cancers are ~30%**
- **Everyone has HPV**
- **Anal Paps are not very good at detecting these pre-cancers**
- **HRA is a better test but expensive**
- **HRA is very well tolerated**

# TRACE STUDY

- **We treat the pre-cancers**
- **Anal cancer is very rare in our treated patients**
- **This screening may work but unproven**

# TCA APPLIED TO AIN 3 LESION



# **PREVENTION OF HPV and HPV-RELATED DISEASES**

# HPV PREVENTION

- **Be monogamous and hope your partner is too**
- **Circumcision**
- **Condoms partially protective**
- **No smoking**
- **Alcohol in moderation**
- **Green tea**
- **Cruciferous vegetables**
- **HPV vaccine if not already multiply HPV-infected**



# SCREENING for ORAL HPV

- Especially in those at risk
- Over age 50 (only two thirds)
- Examine mouth and throat (esp. tonsils) for warts, white patches, lumps



# HPV VACCINES

# HPV VACCINES

## **GARDASIL Quadrivalent Vaccine**

- July 2006
- Females (9-45 y.o.) and Males (9-26 y.o.)
- Warts, CIN, VIN, VaIN, AIS, AIN
- Ano-genital cancers

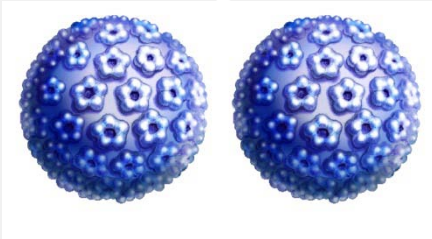
## **CERVARIX Bivalent Vaccine**

- Feb 2010
- Females (10-25 y.o.)
- CIN

# COMPOSITION OF THE BIVALENT HPV VACCINE AND THE QUADRIVALENT HPV VACCINE

## Bivalent HPV vaccine

Antigens



+

AS04 adjuvant

Aluminium salt  
(Al(OH)<sub>3</sub>)

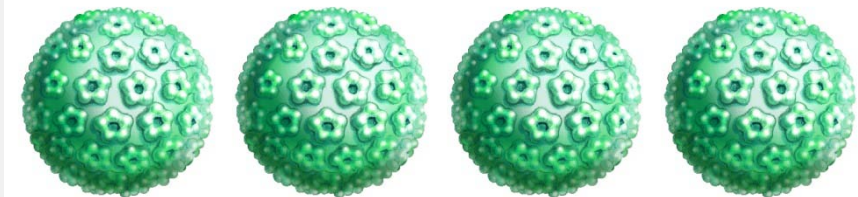
+

MPL  
Immunostimulant

AS04-containing vaccine

## Quadrivalent HPV vaccine

Antigens



+

Adjuvant

Aluminium salt  
(amorphous aluminium  
hydroxyphosphate  
sulphate [AAHS])

AAHS-containing vaccine

# GARDASIL MALE TRIAL: MSM

Per-protocol population (MSM)

	Quadrivalent HPV 6/11/16/18Vaccine (N = 299)			Placebo (N = 299)			Efficacy(%)	p-value <sup>§</sup>
	n	Cases	Rate	n	Cases	Rate		
HPV 6/11/16/18-related <u>AIN</u>	194	5	1.3	208	24	5.8	<b>77.5</b>	< 0.001
By lesion type								
AIN 1	194	4	1.0	208	16	3.9	73.0	
Condyloma Acuminatum	194	0	0.0	208	6	1.4	100	
Non-acuminate	194	4	1.0	208	11	2.6	60.4	
AIN 2 or worse	194	3	0.8	208	13	3.1	74.9	
AIN 2	194	2	0.5	208	9	2.2	75.8	
AIN 3	194	2	0.5	208	6	1.4	63.7	
Anal Cancer	194	0	0.0	208	0	0.0	NA	

\*Cases found from performing an HRA due to the presence of perianal external lesions are not included in this analysis to eliminate potential ascertainment bias. <sup>§</sup> A p-value < 0.0245 (one-sided) corresponds to a lower bound of the confidence interval for vaccine efficacy greater than 0% and supports the conclusion that the vaccine is efficacious against the given endpoint.

N = Number of subjects in the MSM substudy randomized to the respective vaccination group who received at least 1 injection.

n = Number of subjects in the MSM substudy who have at least one follow-up visit after Month 7.

1. Giuliano AR, et al. Presented at EUROGIN 2008, Nice, November 12-15, 2008. Session SS 19-7

2. Palefsky JM et al. N Engl J Med 2011;365:1576-85

# Recommendations: Males 9-26 years

Group	Recommendations		Comments
	Gardasil®	Cervarix™	
Males 9 -26 years	<p>✓ Recommendation Grade A</p> <p>AIN grade 1,2,3 Anal cancer Anogenital warts</p>	<p>Not recommended at this time Grade I</p>	<ul style="list-style-type: none"> <li>▪ Receipt of Gardasil® between 9 and 13 years of age prior to onset of sexual activity is recommended to maximize efficacy of the vaccin.</li> <li>▪ Males between the ages of 14 and 26 years would benefit from Gardasil® if already sexually active as they may not yet have HPV infection, but very unlikely to have been infected with all four HPV types.</li> <li>▪ Should be made aware of the possibility that they are already infected.</li> <li>▪ While Gardasil® is not currently indicated for prevention of penile, perineal, or perianal intraepithelial neoplasia, early clinical trial results show good efficacy (85.6%) against 6-month persistent infection, an important predictor for disease development.</li> </ul>
	<p>✓ Recommendation Grade B</p> <p>Penile, perianal, perineal, neoplasias and associated cancers</p>		
Males who have sex with males (MSM) ≥9 years of age	<p>✓ Recommendation Grade A</p>		<ul style="list-style-type: none"> <li>▪ Early receipt of Gardasil® would confer maximum benefit, since MSM may become infected with HPV more rapidly due to the high rate of infection in the population. Should be made aware of the possibility that they are already infected.</li> </ul>

# RECOMMENDATIONS

- Vaccine most effective if have had few partners
- Even if many partners there may be some benefit
- Why not?
- Cost is an issue – maybe just 2 shots is useful

# SUMMARY

- **HPV is common in many body sites in men**
- **HPV can cause cancers of the mouth and throat, skin, penis and anus.**
- **Men are vectors for penile and anal cancer**
- **The HPV vaccine is effective in men**



**THE END**



# Questions / Comments

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To UNMUTE yourself,  
dial #6

# Thank You!

**WEBINAR 3: 7th Annual BC Gay Men's Health Summit: Reflections on Research and Programming**

Examine the key themes and ideas that emerged during the 150-attendee summit exploring research and programming.

French Only: Wednesday, February 15th, 2012, 2pm EST

**WEBINAR 4: HIV Testing: Different Regions, Different Strategies**

Learn about the newest HIV technologies in use across the country, and the many different ways organizations are working to encourage HIV testing.

English Only: Friday, February 17th, 2012, 2pm EST

**WEBINAR 5: The Rising Tide of Syphilis: Update on Syphilis among Gay, Bisexual, Two-Spirit and other MSM in Canada**

Take a closer look at the epidemiology of syphilis in Canada and find out what you can do to help decrease new infection rates.

English Only: Wednesday, February 22nd, 2012, 2pm EST

