

Low-Risk HPV is NOT No-Risk HPV: Anogenital Warts and Respiratory Papillomatosis in Males



Presenter: Dr. Marc Steben MD, CCFM, FCFM

Chair of the Canadian Network on HPV Prevention
Co-President, HPV Global Action
Family Physician specializing in Sexual Health
Board Member & Education Committee Chair,
International Papillomavirus Society
2023 President, International Society for STD Research



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Moderator: George Wurtak BSc, BEd, MEd

Executive Director, Consortium for Infectious Disease Control
Director, Canadian Network on HPV Prevention
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Moderator



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Webinar Objectives

- Explain low risk HPV natural history
- Compare oral and anogenital (Low Risk) HPV infections between males and females
- Describe burden of disease from anogenital warts and respiratory papillomatosis in males
- Describe prevention methods for anogenital warts, RRP and oral lesions in males
- Counsel males efficiently about HPV vaccination

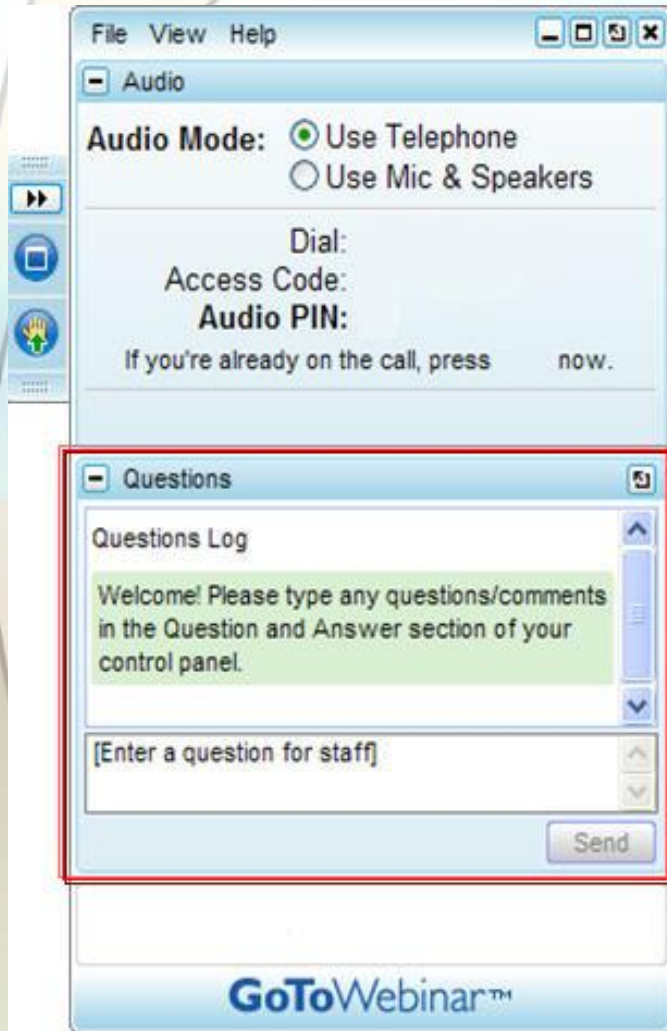
Administrative Information

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- Submit questions at any time by typing in the "Questions" pane on the control panel & click 'Send' button
- Questions will be answered at the end of the presentation

NOTE: For **mobile device** users:

- To open the questions pane, tap on the "?" or "Questions"
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Note: A recording of the presentation will be made available at www.CIDCgroup.org

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www.CIDCgroup.org

Complete the Evaluation Survey at:

https://bit.ly/Low_risk_HPV

Completion of survey is requested to receive a certificate of participation

– all registered participants will receive an email with this link

Presenter



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Low-risk HPV is NOT no-risk HPV! And anogenital warts are not so benign even in males!

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I am a member of a Speaker Bureau.	Merck, GSK
I have received payment from a commercial organization (including gifts or other consideration or 'in kind' compensation).	Bayer, Lupin, GSK, Paladin, Roche molecular systems, Merck.
I have received a grant(s) or an honorarium from a commercial organization.	Abbott, Bayer, Beckton-Dickinson, Biofire, Gen-Probe/Hologic, GSK, Laboratoire Biron, Lupin, Merck/Merck Sharp Dohme/Sanofi-Pasteur, Paladin, Roche molecular systems.
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I hold investments in a pharmaceutical organization, medical devices company or communications firms.	I own a communication company (Communications Action-Santé Inc.)
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Learning Objectives

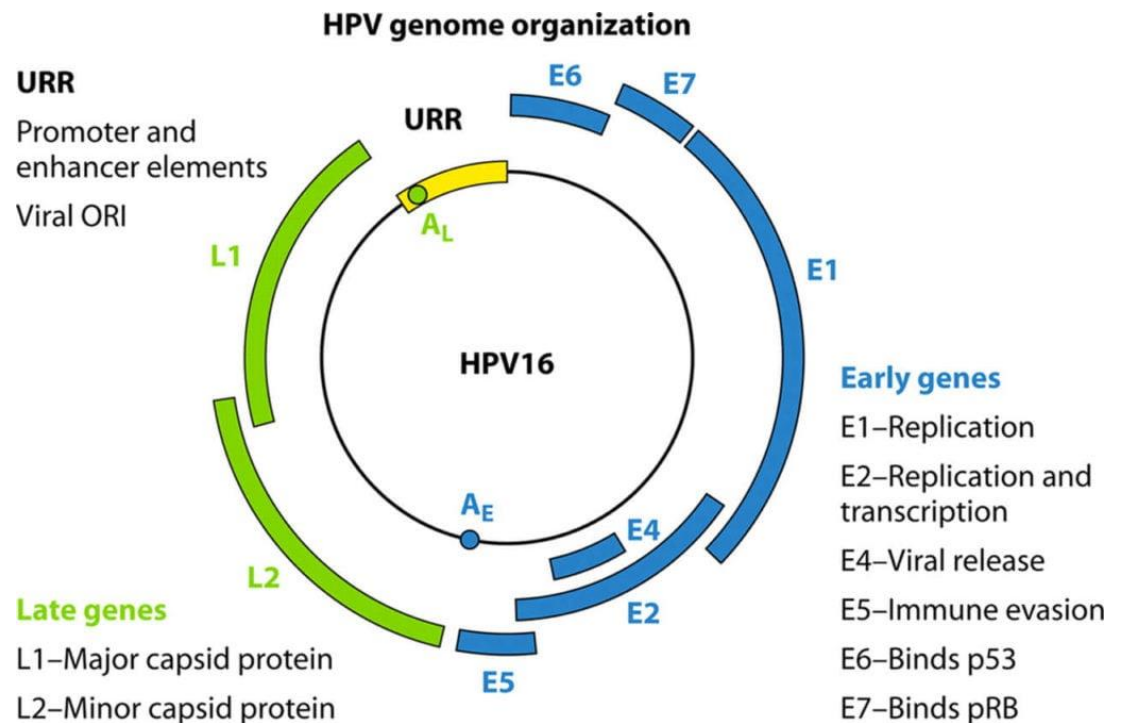
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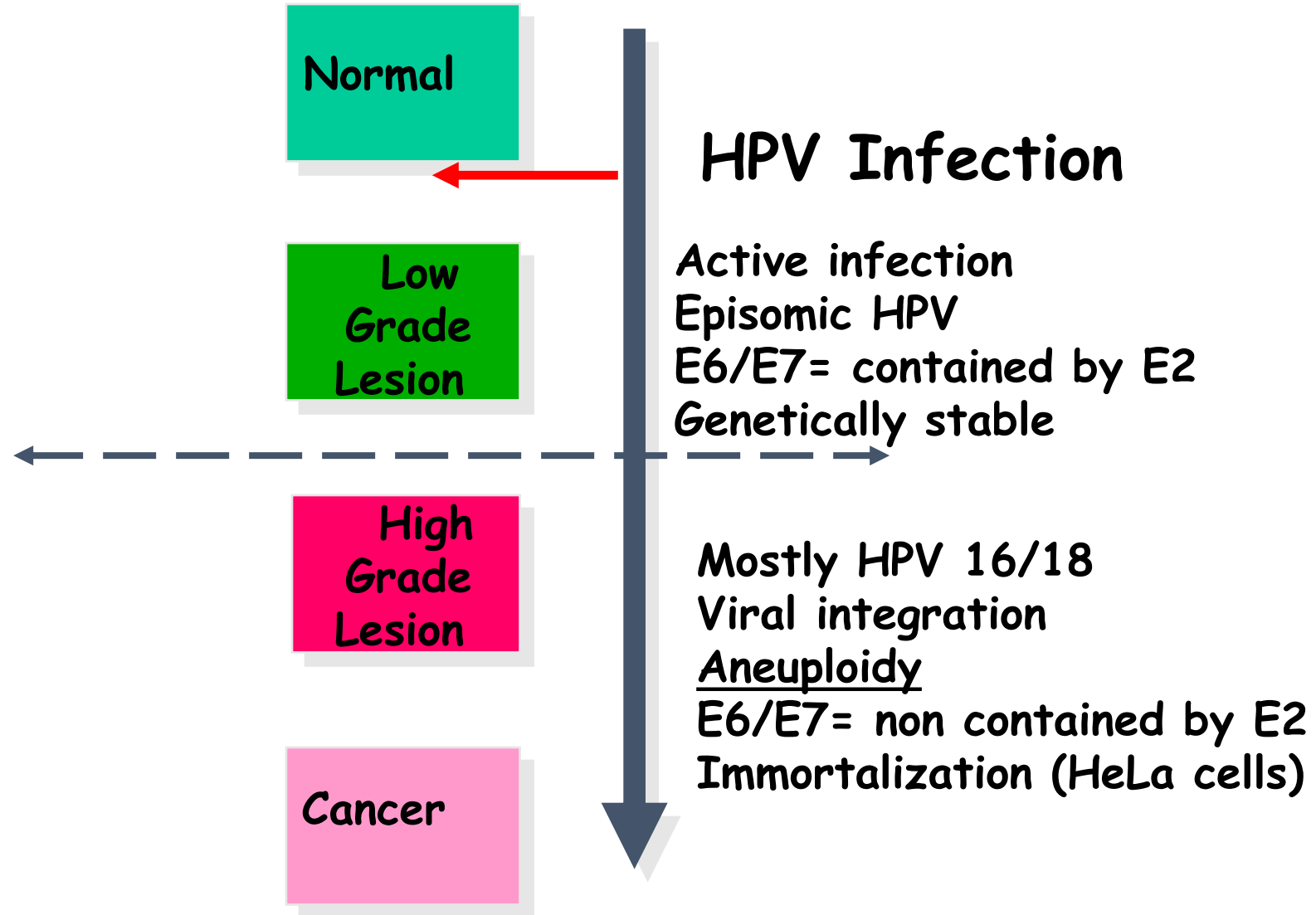
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LR HPV vs HR HPV

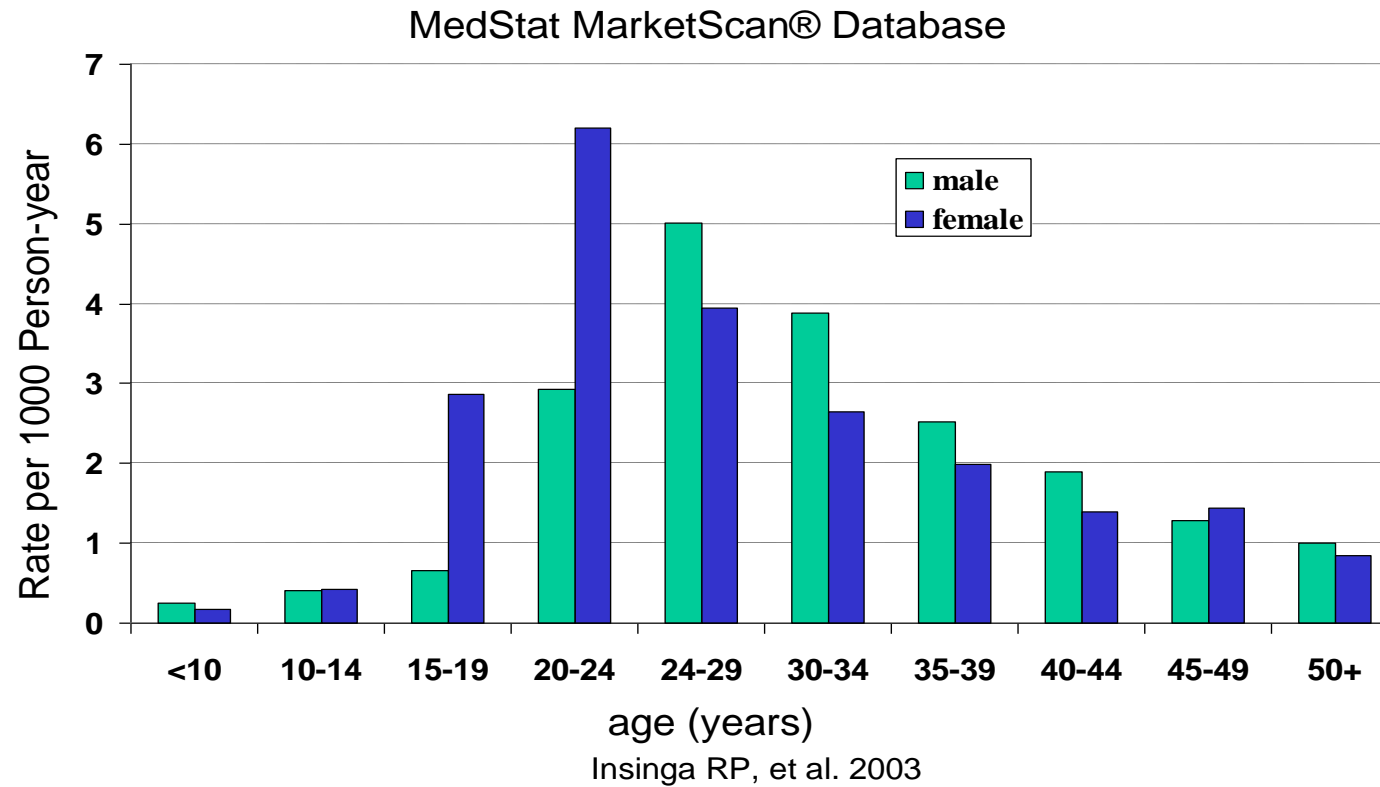
- Low-risk HPVs
 - mostly cause no disease
 - few low-risk HPV types can cause warts on or around the genitals, anus, mouth, or throat
 - Low risk HPV can be found coincidentally in cancer
 - Very rarely integrated in cancer in such cases
- High-risk HPVs
 - can cause several types of cancer
 - about 14 high-risk HPV types including HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68.
 - two of these, HPV16 and HPV18, are responsible for most HPV-related cancers.
 - promote the disruption of normal cell-cycle control
 - ability to target the retinoblastoma (Rb) family of proteins and p53 and to induce telomerase are some of the critical events that contribute to the development of malignancy.



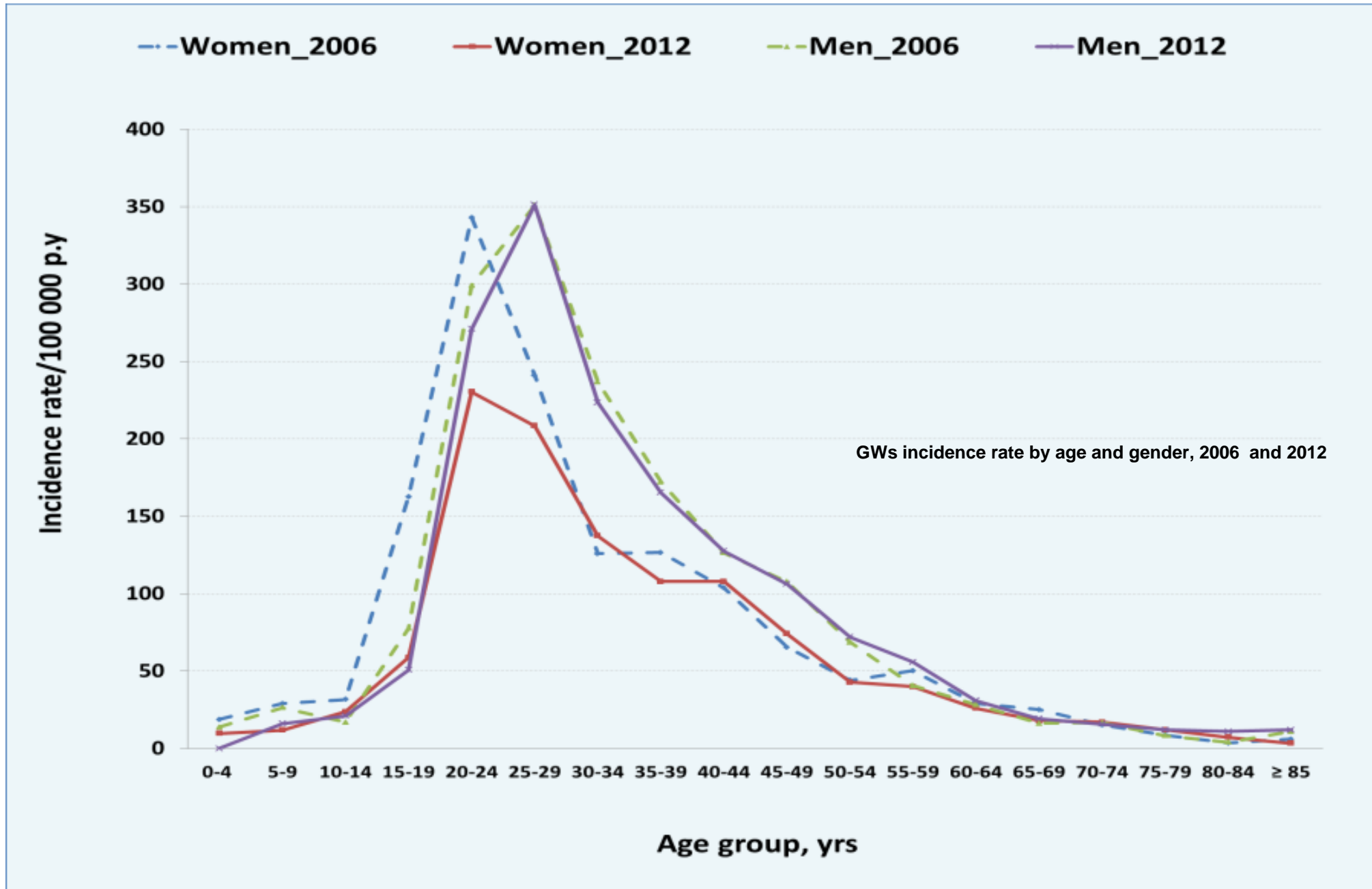
Progression to cancer



USA EGW Incidence rate



Quebec Results on Provincial drug plan



Ano-genital warts in Québec province from the provincial drug benefit plan data

- 24,267 individuals had at least one episode between 1998 and 2007 versus
- 21,411 between 2009 and 2012.
- 10% had more than 1 episode in the first period
 - 12% of ♂ and
 - 8% of ♀

Incidence of genital warts when HPV 6-11 university students, San Francisco

Women

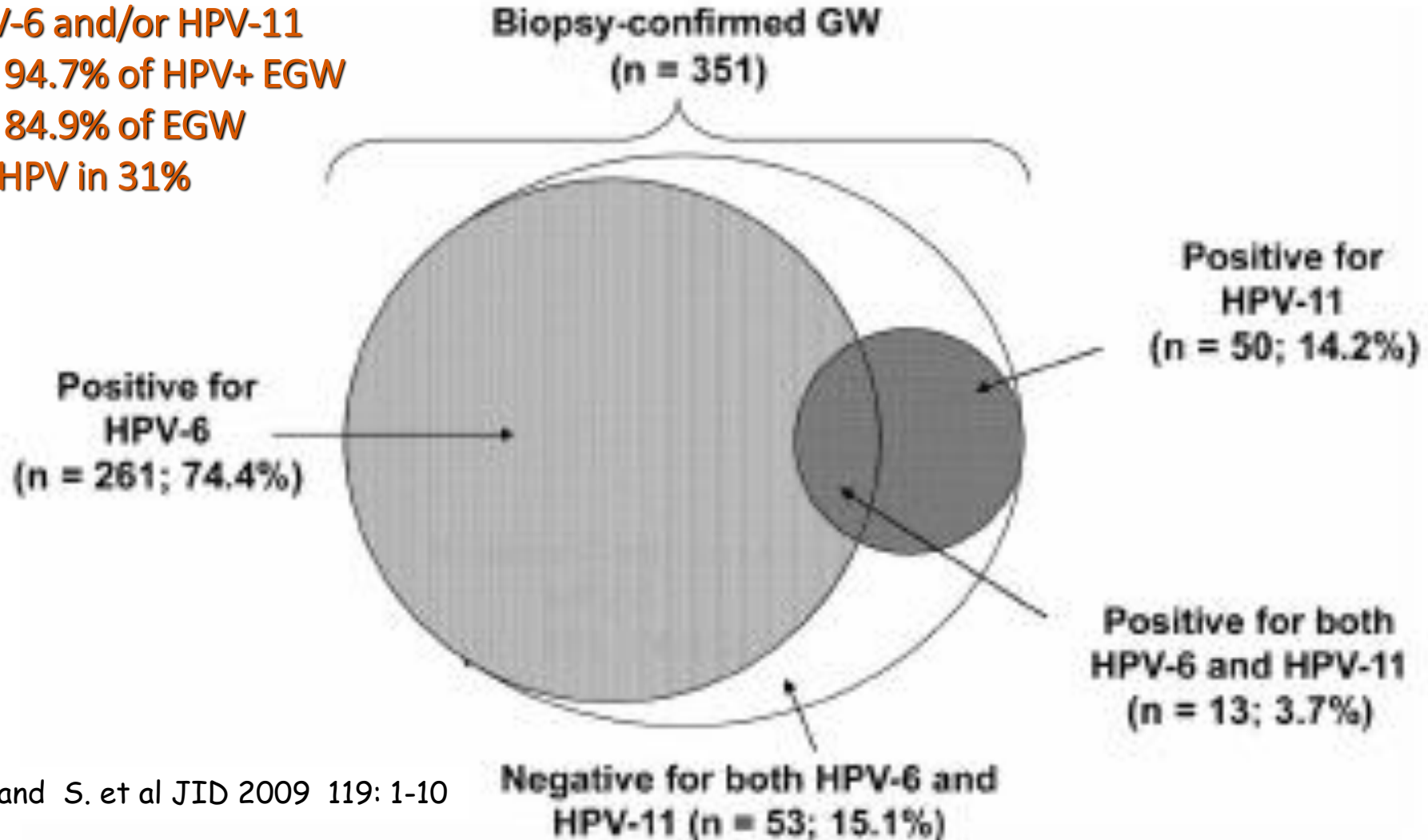
- 36-months cumulative incidence
= 64.2%

Men

- 24-months cumulative incidence
= 57.9%

Natural history of EGW in the placebo group of FUTURE I AND II trials

- HPV-6 and/or HPV-11
- in 94.7% of HPV+ EGW
- in 84.9% of EGW
- HR HPV in 31%

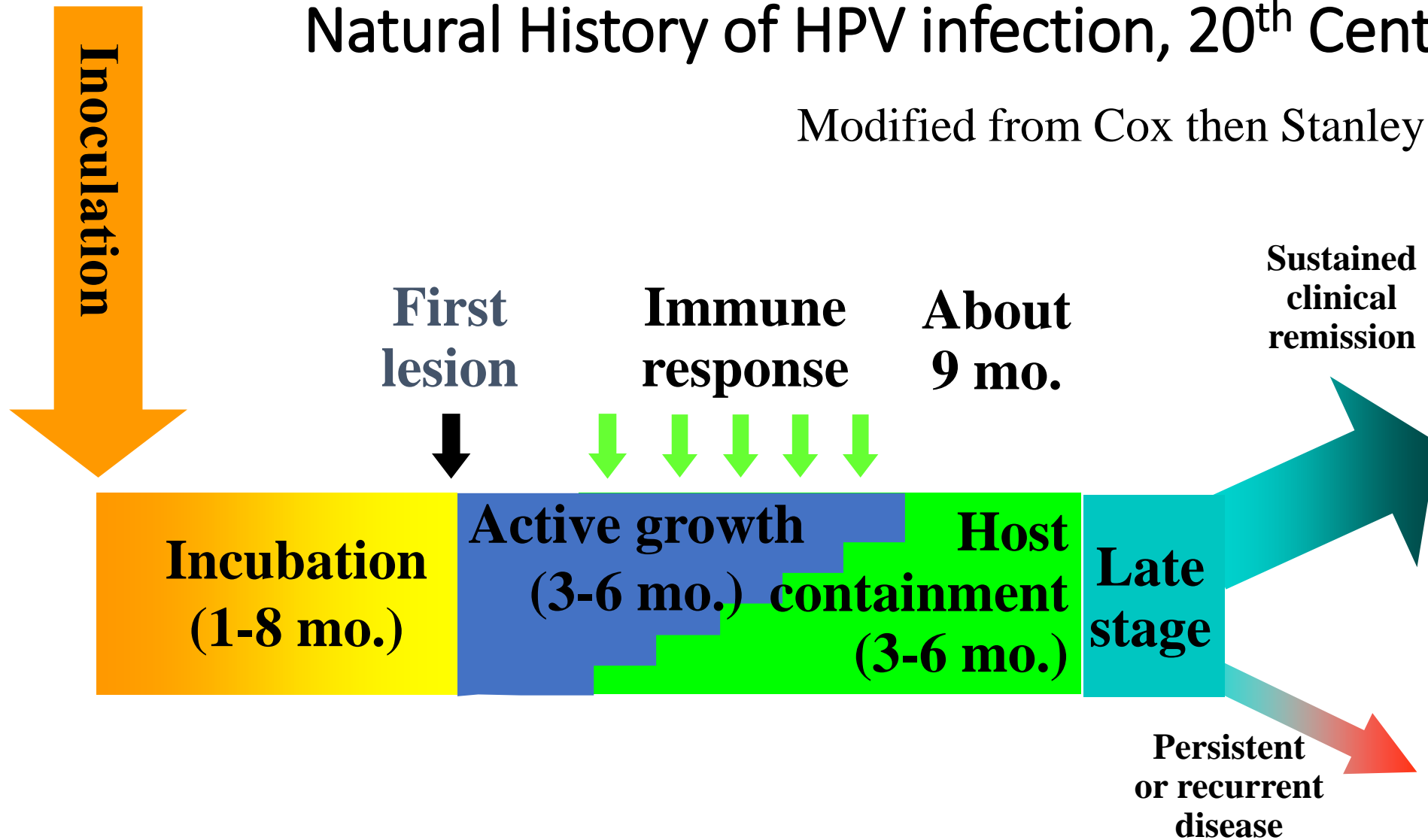


Natural history of EGW in the placebo group of FUTURE I AND II trials

- 2530 women sero- for HPV-6 on day 1
 - 12.4% developed antibodies to HPV-6
 - Of those, 19.4% received a diagnosis of GW during the course of the study,
 - with 90.2% were HPV-6+.
- 2663 women sero- for HPV-11 on day 1
 - 3.8% developed antibodies to HPV-11
 - Of those, 19.6% were diagnosed with GW during the course of the study,
 - with 90.0% were HPV-11+.

Natural History of HPV infection, 20th Century

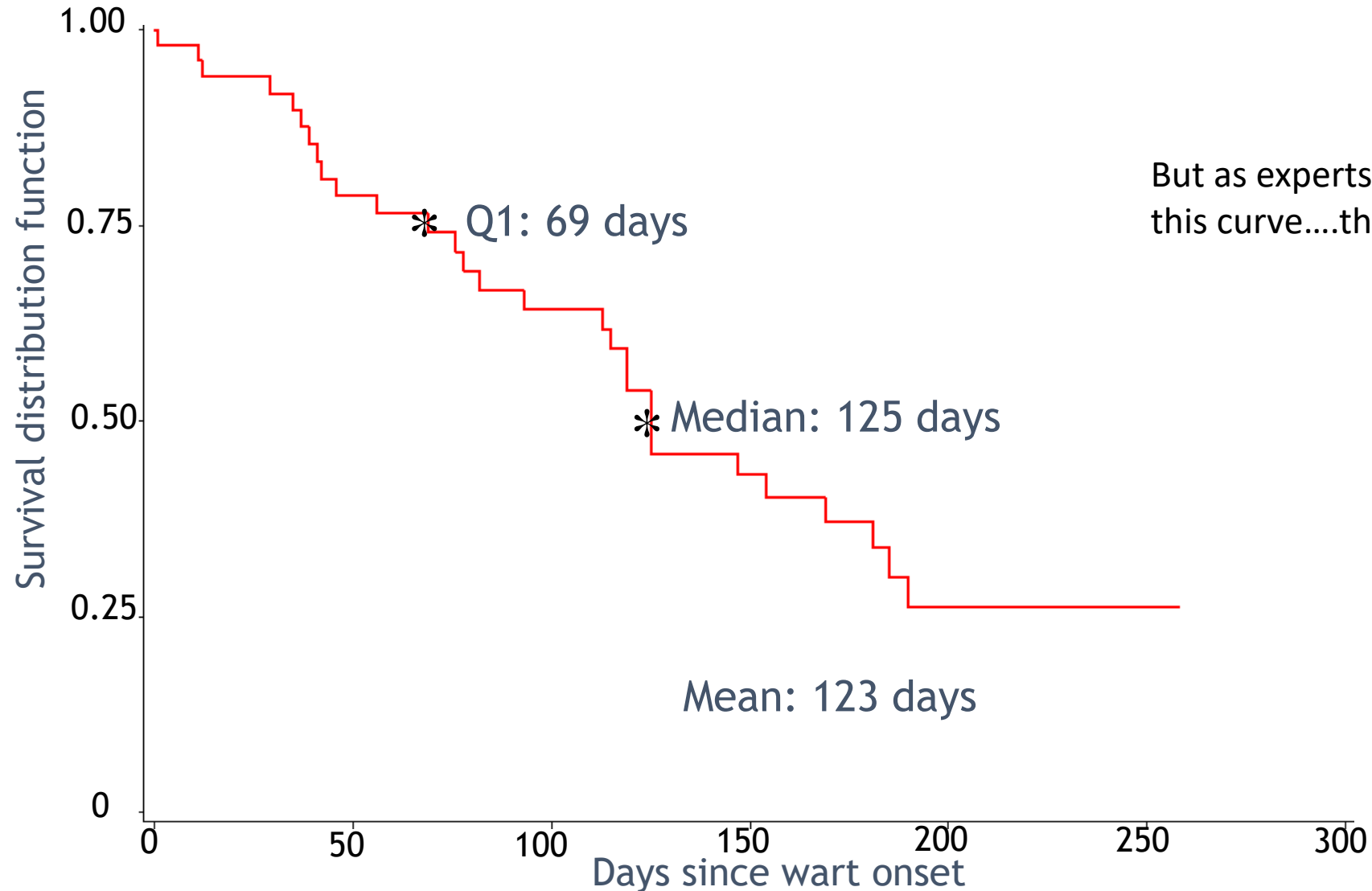
Modified from Cox then Stanley



- There is no therapeutic antiviral option
- Most options destroy the lesions not the virus

Duration of the first wart episode

PISCES study, Drolet et al



But as experts, we see the tail end of this curve...the long wart treatment!

Persistent or recurrent HPV infection or lesion

**Sustained
clinical
remission**

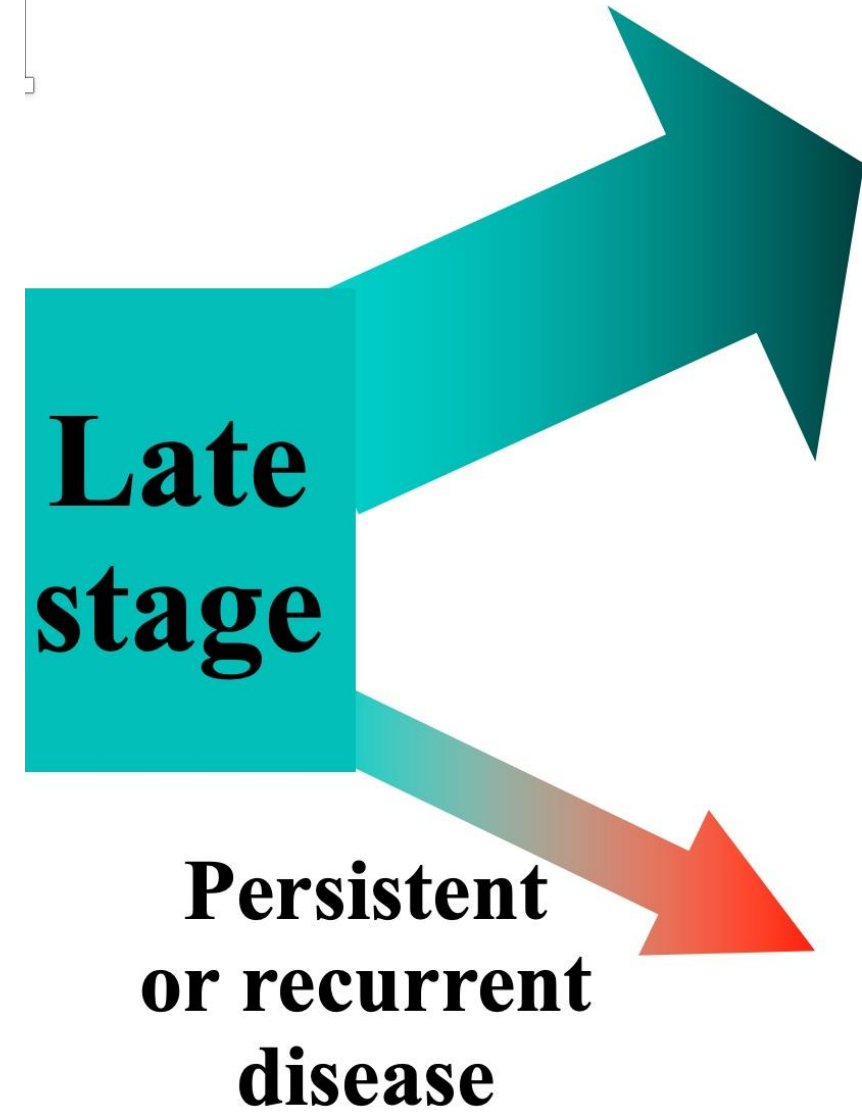
A) Relative immunodeficiency:

- Pregnancy
- Chronic disease: HIV, diabetes, renal insufficiency...
- Smoking

B) Iatrogenic immunodeficiency :

- Transplant or cancer treatments
- Immunomodulator:
- Prednisone
- Methotrexate
- Calcineurin blockers

C) Immunosenescence



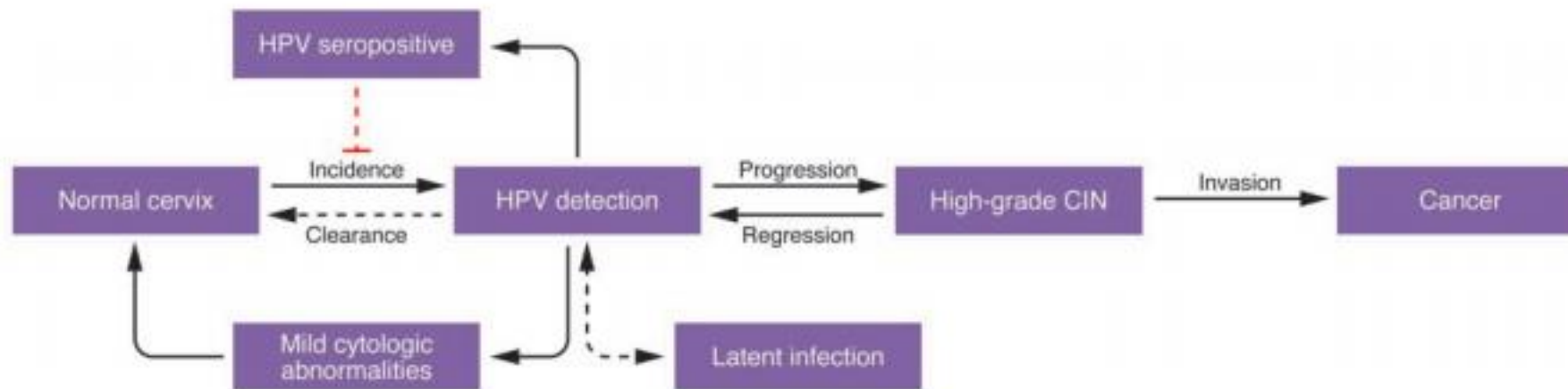
Incidence, Duration, and Reappearance of Type-Specific Cervical Human Papillomavirus Infections in Young Women

Ralph P. Insinga¹, Gonzalo Perez², Cosette M. Wheeler³, Laura A. Koutsky⁴, Suzanne M. Garland⁵, Sepp Leodolter⁶, Elmar A. Joura⁶, Daron G. Ferris⁷, Marc Steben⁸, Darron R. Brown⁹, Elamin H. Elbasha¹, Jorma Paavonen¹⁰, and Richard M. Haupt¹; for the FUTURE I Investigators

Table 4. Reappearance of cervical HPV-6,11, 16, 18, 31, 33, 35, 45, 52, 58, and 59 infections following a period nondetection

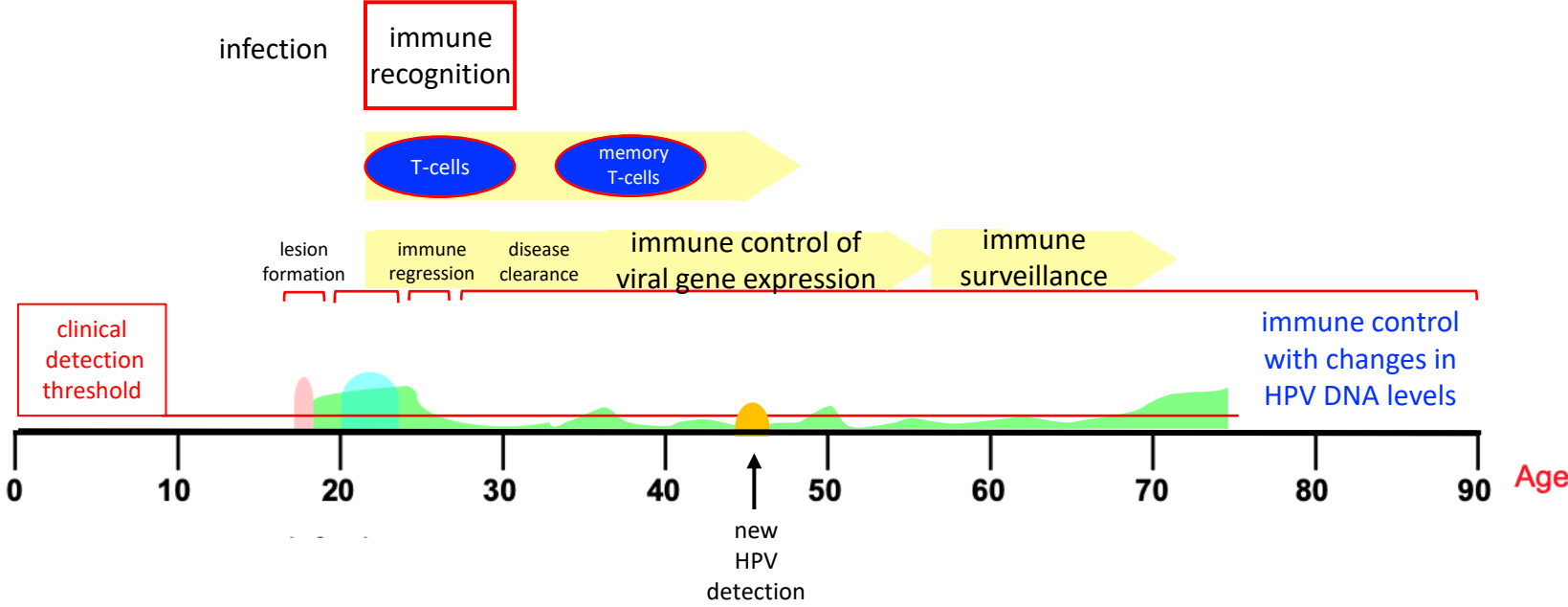
HPV type (<i>n</i> = 827)	Proportion of infections reappearing by 12 mo* (95% CI)	Proportion of infections reappearing by 24 mo* (95% CI)	Proportion of infections reappearing by 36 mo* (95% CI)
HPV-6 (<i>n</i> = 89)	0.0 (–)	1.7 (0.2-11.2)	16.1 (5.6-41.1)
HPV-11 (<i>n</i> = 11)	9.1 (1.3-49.2)	9.1 (1.3-49.2)	9.1 (1.3-49.2)
HPV-16 (<i>n</i> = 162)	6.6 (3.6-11.9)	7.5 (5.2-13.3)	11.0 (6.1-19.4)
HPV-18 (<i>n</i> = 70)	5.8 (2.2-14.8)	8.8 (3.5-20.8)	8.8 (3.5-20.8)
HPV-31 (<i>n</i> = 112)	6.8 (3.3-13.7)	6.8 (3.3-13.7)	6.8 (3.3-13.7)
HPV-33 (<i>n</i> = 33)	3.0 (0.4-19.6)	7.9 (1.9-29.0)	7.9 (1.9-29.0)
HPV-35 (<i>n</i> = 26)	0.0 (–)	0.0 (–)	0.0 (–)
HPV-45 (<i>n</i> = 53)	3.8 (1.0-14.3)	3.8 (1.0-14.3)	3.8 (1.0-14.3)
HPV-52 (<i>n</i> = 100)	6.4 (2.9-13.6)	6.4 (2.9-13.6)	6.4 (2.9-13.6)
HPV-58 (<i>n</i> = 55)	2.3 (0.3-15.4)	2.3 (0.3-15.4)	2.3 (0.3-15.4)
HPV-59 (<i>n</i> = 116)	5.4 (2.5-11.7)	7.5 (3.4-16.0)	7.5 (3.4-16.0)

*These monthly intervals refer to time from the date of the second negative cervical swab following the initial infection. The actual time from infection nondetection corresponding to these data is therefore ~8 mo longer (is 9-21, 21-33, and 33-45 mo following nondetection).

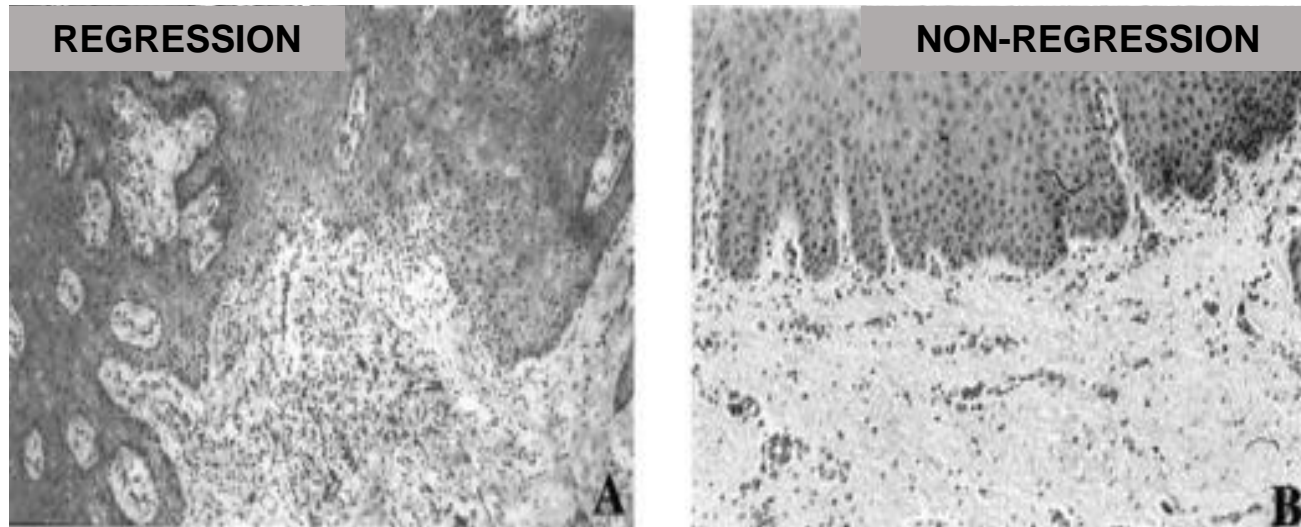


Current Thinking

21st Century Natural History of Infection During a Woman's Lifetime



Events leading to disappearance of AGW



- 125 patients
- Spontaneous regression in 14 patients
- Biopsies demonstrated a cellular type immune reaction with activation markers
- Conclusion: treatment that would reproduce this reaction would heighten the efficacy of immuno- intervention against HPV infection the genital tract level

Coleman N, Birley HD, Renton AM, Hanna NF, et al. [Immunological events in regressing genital warts.](#) (PMID:7801889) American Journal of Clinical Pathology[1994, 102(6):768-774]

Genital Warts and Risk of Cancer: A Danish Study of Nearly 50 000 Patients With Genital Warts

Maria Blomberg,¹ Soren Friis,¹ Christian Munk,¹ Andrea Bautz,¹ and Susanne K. Kjaer^{1,2}

¹Institute of Cancer Epidemiology, Danish Cancer Society, and ²Gynecological Clinic, Rigshospitalet, University of Copenhagen, Denmark

Background. We conducted a large national cohort study to examine the risk of cancer among men and women with genital warts (GW).

Methods. By use of the Danish National Patient Register, we identified 16,155 men and 32,933 women who received a diagnosis of GW during 1978–2008. Standardized incidence ratios (SIRs) were computed as estimates of the relative risk of specific cancers or sites.

Results. A diagnosis of GW was strongly related to anal (SIR for men, 21.5; SIR for women, 7.8), vulvar (SIR, 14.8), vaginal (SIR, 5.9), cervical (SIR, 1.5), penile (SIR, 8.2), and head and neck cancer (SIR, 2.8), including subsites of head and neck cancer with confirmed HPV association (SIR for men, 3.5; SIR for women, 4.8). The risks remained elevated for >10 years following GW diagnosis. In addition, we found moderately increased SIR estimates for nonmelanoma skin cancer, smoking-related cancers, and Hodgkin and non-Hodgkin lymphoma.

Conclusions. Individuals with GW have a long-term increased risk of anogenital cancers and head and neck cancers. The elevated risks of nonmelanoma skin cancers might indicate an association with HPV, while excess risks of other cancers could point to differences in other risk factors between individuals with GW and the

Genital warts as indicator of future cancer

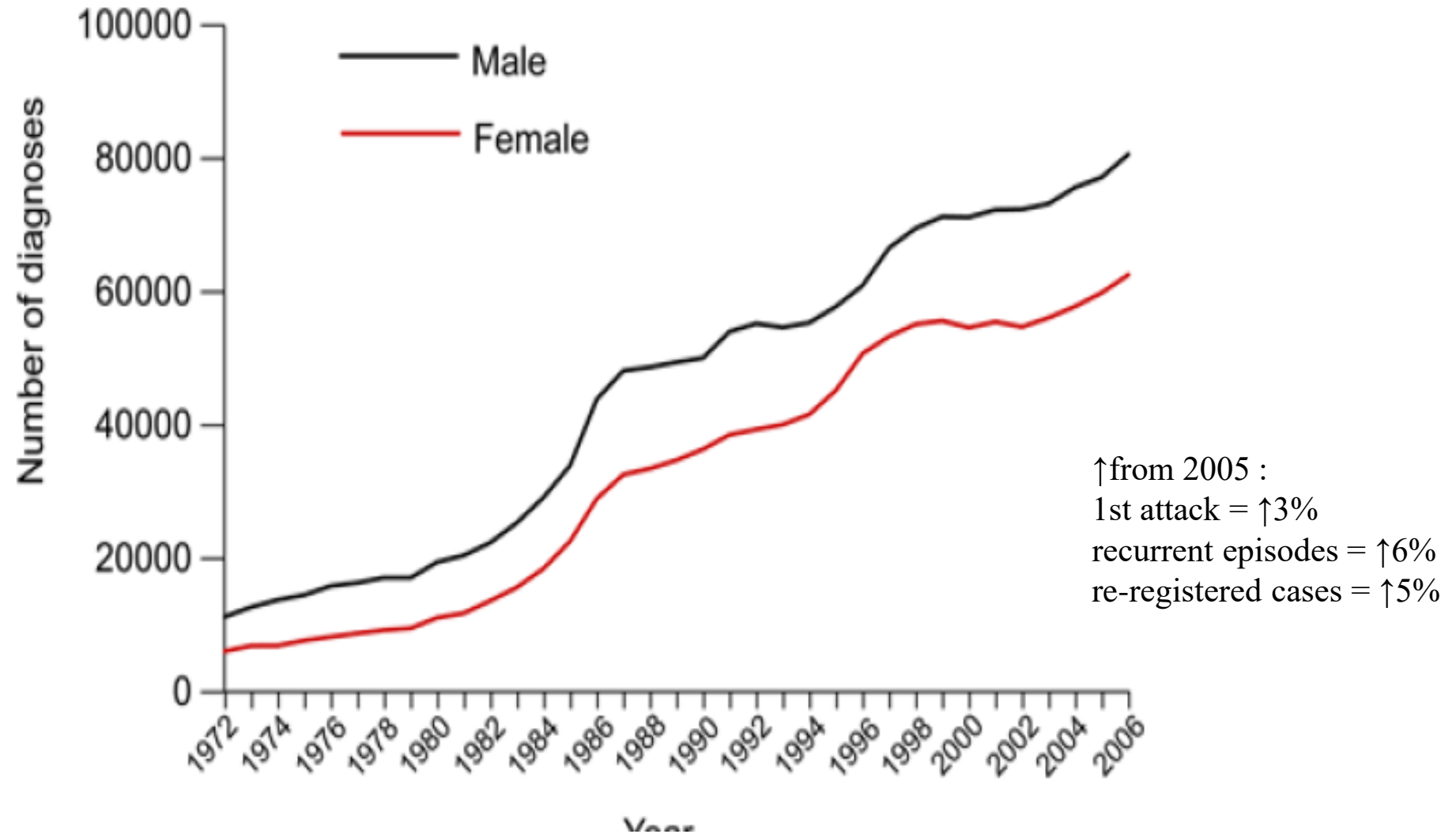
Table 1. Standardized Incidence Ratios (SIRs) of Cancer Among Men and Women Who Received a Diagnosis of Genital Warts in Denmark During 1978–2009

Cancer site	Men			Women			All		
	Observed	SIR	95 % CI	Observed	SIR	95 % CI	Observed	SIR	95 % CI
All cancers	815	1.5	1.4–1.6	1548	1.2	1.2–1.3	2363	1.3	1.3–1.4
All smoking-related cancers ^a	255	1.8	1.6–2.1	407	1.9	1.7–2.1	662	1.9	1.7–2.0
All HPV-related cancers ^b	60	7.2	5.5–9.2	245	2.8	2.4–3.1	305	3.1	2.8–3.5
Anogenital									
Cervix uteri				117	1.5	1.3–1.8	117	1.5	1.3–1.8
Vagina				6	5.9	2.2–12.9	6	5.9	2.2–12.9
Anus	29	21.5	14.4–30.9	33	7.8	5.4–11.0	62	11.1	8.5–14.3
Vulva				74	14.8	11.7–18.6	74	14.8	11.7–18.6
Penis	11	8.2	4.1–14.6				11	8.2	4.1–14.6

Learning Objectives

- Explain low risk (LR) HPV natural history
- **Compare anogenital LR HPV infections between males and females**
- Describe burden of disease from anogenital warts and respiratory papillomatosis in males
- Describe prevention methods for anogenital warts, RRP and oral lesions in males
- Counsel males efficiently about HPV vaccination

Figure 1 Diagnoses of genital warts (first, recurrent and re-registered) seen in GUM clinics in England, Wales and Scotland: 1971 to 2006



Results

- **Women**
 - Significant decline of incidence
 - 45 % ($p < 0.0001$) <20
 - 19 % ($p < 0.0001$) in 20-24.
 - Small decline in ≥ 25 .
 - Peak incidence in 20-24 decreased from 343 in 2006 to 230/100 000 p-y in 2012.
- **Men**
 - Small but significant decline of 21% ($p = 0.004$) in men < 20.
 - No change in peak incidence in men

Age-specific incidence rates and rate ratios of GWs during pre-vaccine (2004-2007) and vaccine (2009-2012) periods

	2004-2007 Period 1 (P1)	2009-2012 Period 2 (P2)	Rate ratio P2/P1 (95% CI)
Women			
< 20 yrs	65.43	36.47	0,55 (0.48-0.63)
20-24	335.95	274.73	0.81 (0.75-0.88)
25-29	232.68	207.7	0.89 (0.81-0.98)
≥ 30	45.06	41.26	0.91 (0.86-0.97)
Overall¹	102.5	87.9	0.86
Men			
< 20 yrs	34.68	27.56	0.79 (0.76-0.93)
20-24	298.37	293.95	0.99 (0.98-1.08)
25-29	319.62	315.60	0.98 (0.90-1.07)
≥ 30	69.61	66.63	0.95 (0.90-1.00)
Overall¹	117.6	117.6	1.00

GWs incidence rate by age and gender, 2006 and 2012

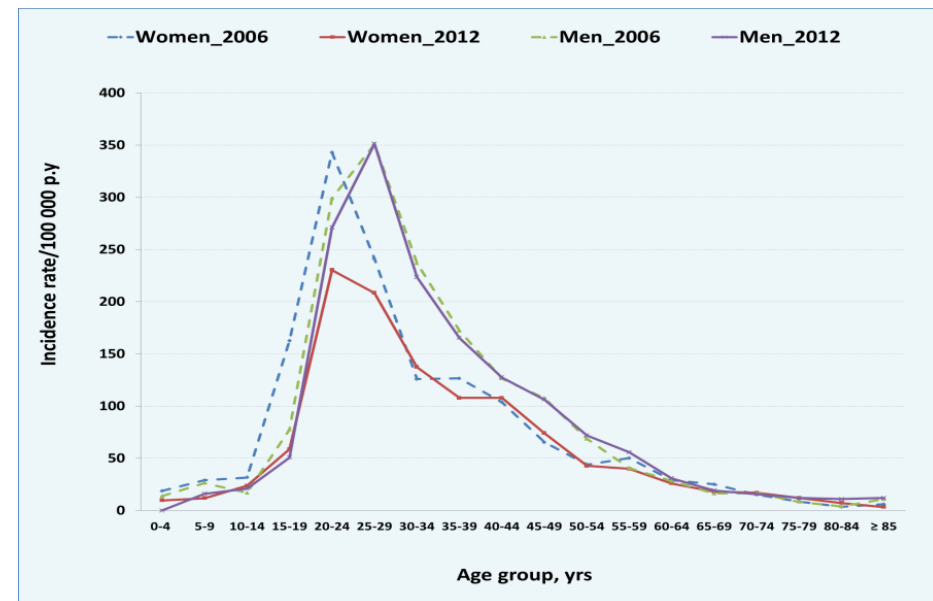
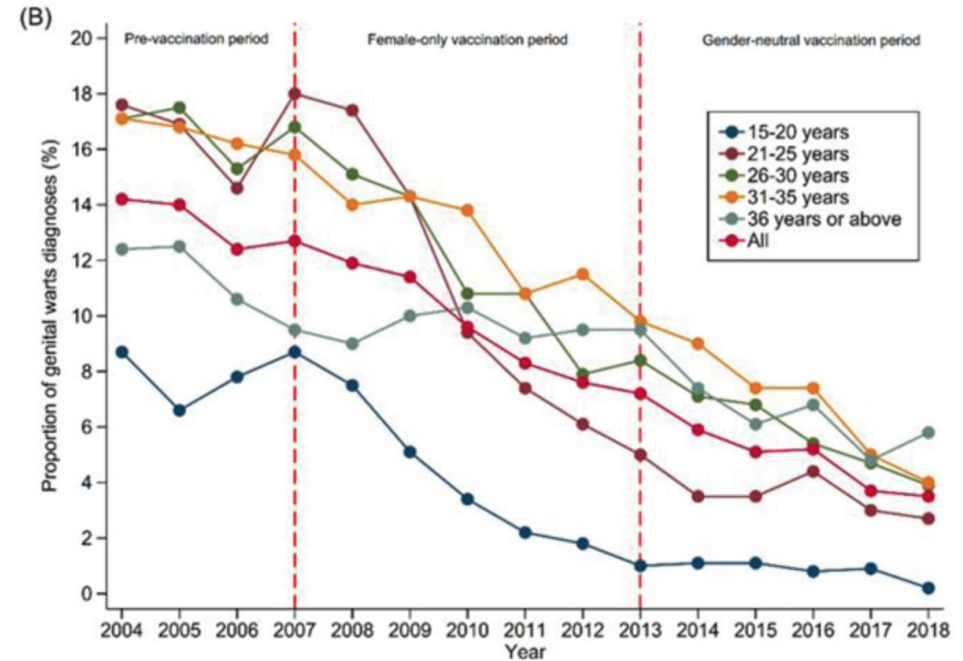
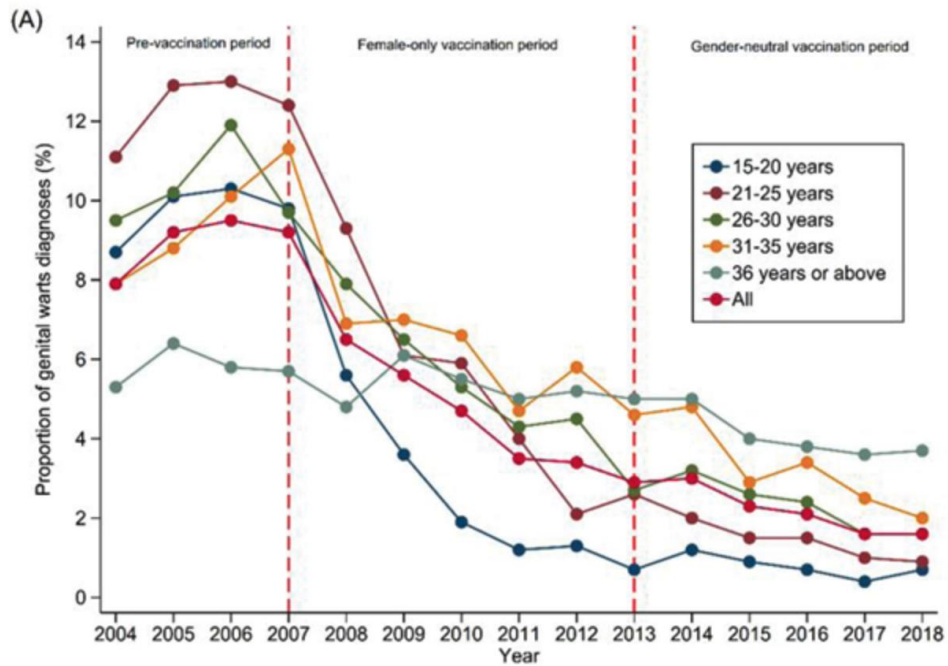


Figure 1

Proportions of genital wart diagnoses in Australian-born female (A) and heterosexual male (B) individuals attending a network of sexual health clinics between 2004 and 2018¹





Burden of HPV-Related Recurrent Diseases in Females



Disease	Study Description	Burden of Recurrence	Time to Recurrence
Post-LEEP Persistent HPV Infection	Meta-analysis of 25 studies estimating incidence of HPV infection and subsequent disease after treatment for CIN ¹	Up to 24%	>6 to 36 months
Post-LEEP [L SEP] High-Grade Cervical Disease	Meta-analysis estimating recurrence of high-grade cervical lesions following excisional treatment for CIN 2+ ²	~7%	Within 2 years
Genital Warts	Retrospective study estimating genital wart recurrence in Australian females ³	~30% with at least 1 recurrent GW	3 years
	Retrospective chart review estimating genital wart recurrence in high-risk adults in Quebec ⁴	47% with 1 recurrent GW	4 years
Post-Treatment Vulvar disease	Population-based case-control study of women with VIN3 ⁵	~34% with recurrent VIN. 73.4% recurred within 3 years	Up to 5 years

1. Rositch AF, et al. *Gynecol Oncol.* 2014;132(3):767-779. 2. Arbyn M, et al. *The Lancet Oncology.* 2017;18(12):1665-1679. 3. Widschwendter A, et al. *Arch Gynecol Obstet.* 2019;300(3):661-668. 4. Thomas R, et al. *Sex Transm Dis.* 2017;44(11):700-706. 5. Madeleine MM et al. *J Low Genit Tract Dis* 2016;20: 257-260.



Burden of HPV-Related Recurrent Diseases in Males

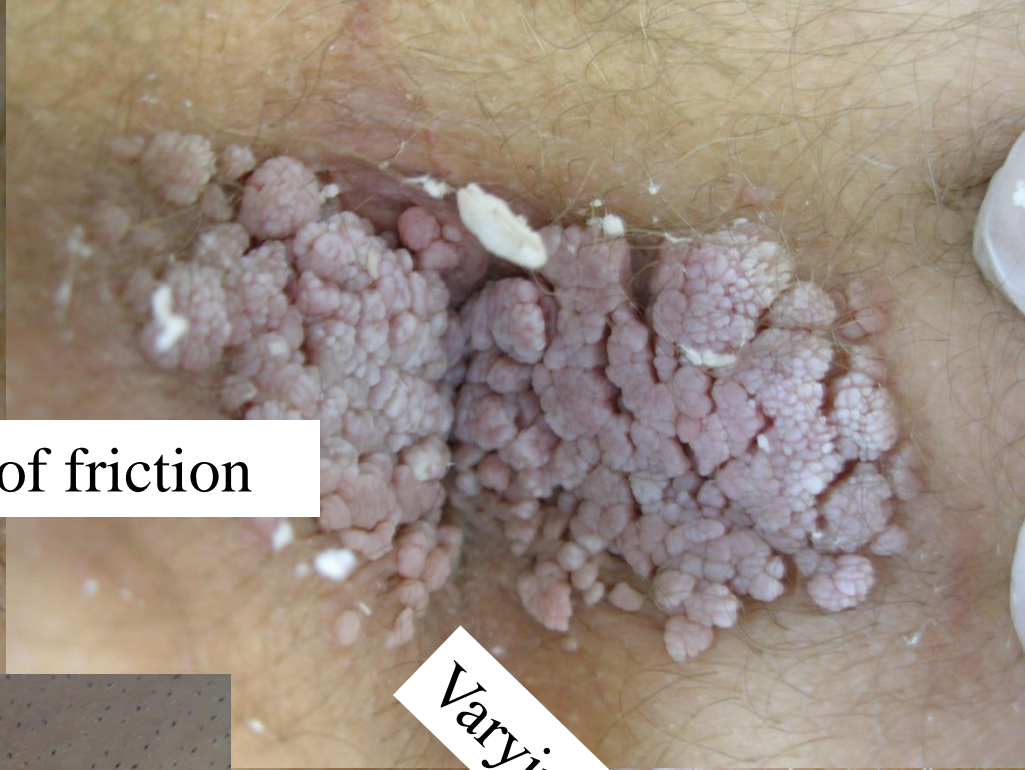


Disease	Study Description	Burden of Recurrence	Time to Recurrence
Genital Infection and Warts in Males [LIM] (HIM Study)	HPV-type specific genital HPV infection recurrence in males ¹	20% incident, 31% prevalent	3.7 years
	Genital wart recurrence in males ²	44% with at least 1 recurrent GW	4 years
Genital Warts	Retrospective chart review estimating genital wart recurrence in high-risk adults in Quebec ³	~49%	4 years
High-Grade Anal Neoplasia in MSM	Risk of recurrence following treatment for anal HSIL in HIV-infected MSM ⁴	23.5%	After 1 year
		53.5%	After 2 years
High-Grade Anal Neoplasia in MSM	Risk of recurrence following treatment for anal HSIL in HIV-infected MSM ⁵	53%	After 1 year
		68%	After 2 years

1. Pamnani SJ, et al. Recurrence of Genital Infections With 9 Human Papillomavirus (HPV) Vaccine Types (6, 11, 16, 18, 31, 33, 45, 52, and 58) Among Men in the HPV Infection in Men (HIM) Study. *J Infect Dis.* 2018;218(8):1219-1227. 2. Giuliano AR, et al. Genital Wart Recurrence Among Men Residing in Brazil, Mexico, and the United States. *J Infect Dis.* 2019;219(5):703-710. 3. Thomas R, et al. Recurrence of Human Papillomavirus External Genital Wart Infection Among High-Risk Adults in Montreal, Canada. *Sex Transm Dis.* 2017;44(11):700-706. 4. Burgos J, Curran A, Landolfi S, et al. Risk factors of high-grade anal intraepithelial neoplasia recurrence in HIV-infected MSM. *AIDS.* 2017;31(9):1245-1252. 5. Goldstone SE, Johnstone AA, Moshier EL. Long-term outcome of ablation of anal high-grade squamous intraepithelial lesions: recurrence and incidence of cancer. *Dis Colon Rectum* 2014; 57:316-323.

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Areas of friction



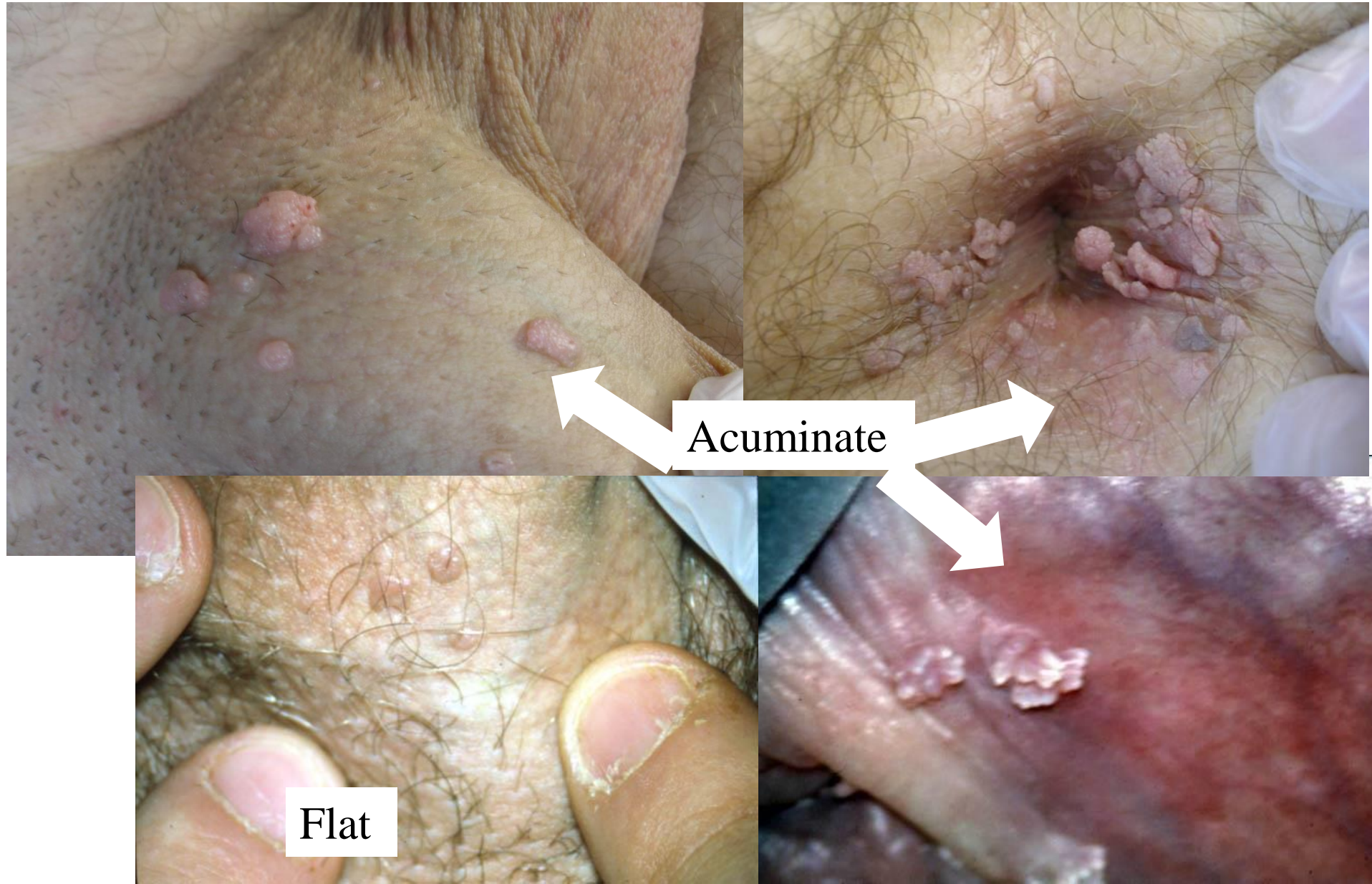
Asymmetrical



Varying #

Clinical presentation

External ano-genital warts



Normal variations

- In both sexes: sebaceous glands
- In women: vestibular papillae, also known as micropapillomatosis labialis
- In men: pearly penile papules on the coronal sulcus

Homogeneous
and symmetrical



Sebaceous glands



Sebaceous glands



Pearly papules



Micropapillomatosis labialis

Pathologic entities

- Infections
 - Secondary syphilis with condylomata lata
 - *Molluscum contagiosum*
- Diseases of the skin and mucosa
 - Intradermal nevi
 - Skin tags
 - Seborrheic keratoses
- Cancer
 - Intraepithelial neoplasia



Summary of treatment options for genital warts

- **Genital wart treatment may be associated with**
 - **Considerable discomfort, erythema, epithelial erosion, ulceration, depigmentation, scarring³**
 - **Embarrassing, painful, and uncomfortable⁴**
 - **Lengthy duration of some therapies³**

Comparison of Treatments for Genital Warts*,¹		
Treatment	Clearance Rate (%)	Risk of Recurrence (%)
Cryotherapy	60–90	20–40
Imiquimod	30–50	15
Interferon	20–60	†
Laser treatment	25–50	5–50
Podofilox	45–80	5–30
Podophyllin resin	30–80	20–65
Surgical excision	35–70	20
Trichloroacetic acid	50–80	35

¹ Wiley DJ et al. Clin Infect Dis 2002;35 (suppl 2): S210–24. ² Akom E Venne S. Institut National de Sante publique du Quebec Nov. 2002.

³ Kodner CM, Nasraty S. Am Fam Physician 2004;70:2335–42. Maw RD et al. Int J STD AIDS 1998; 1998:571–8

Summary of treatment options for genital warts

		Comparison of Treatments for	
<ul style="list-style-type: none"> • Prim sympt • Treat not t • Geni with • • • • • • • 	<p>Comparisons between treatment modalities are difficult to make:</p> <ul style="list-style-type: none"> • Not the same inclusion/exclusion criteria • Length of follow-up • Not the same definition of clearance 		Risk of recurrence (%)
			20–40
			15
			†
			5–50
			5–30
			20–65
			20
			35
			Trichloroacetic acid

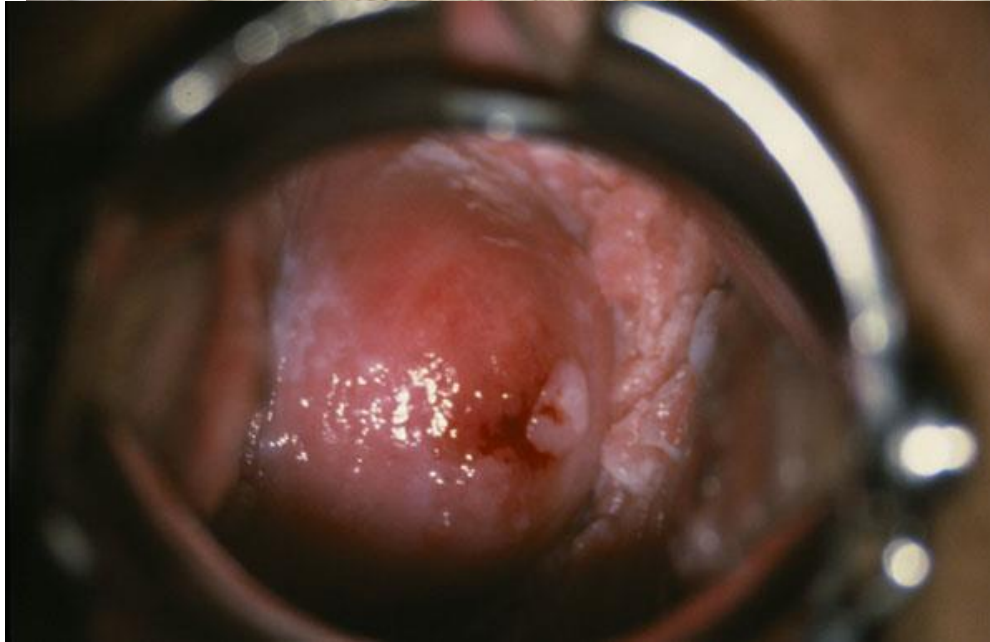
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Treatment to be self applied at home

<p>Podophyllotoxin Solution (or gel) Wartec™ Condyline™.</p>	<p>BID for 3 days per week with 4 days without treatment Total of 6 weeks</p>	<p>Application by small plastic spatula or small cotton tip applicators or with finger</p>	<p>Do not apply to uterine cervix, meatus, vagina or in the anus. Contraindicated during pregnancy Difficult for patients to assess maximum dose</p>
<p>Imiquimod cream 5% Aldara™</p>	<p>3 times per week with at least one day off in between doses Up to 16 weeks</p>	<p>One full envelop per application Apply in thin coat Rub until absorbed by the skin Wash the area 6-8 hours after application</p>	<p>Do not apply to uterine cervix, meatus, vagina or in the anus. Not approved for use in pregnancy</p>
<p>Sinecatechin 15% ointment Veregen®</p>	<p>3 times per day Up to 16 weeks The maximum recommended human dose was set at 3 times daily topical administration of 250 mg total 750 mg containing 112.5 sinecatechins</p>	<p>0.5 cm strand of ointment to each wart dabbing it on to ensure complete coverage leaving a thin layer. No need to wash prior the next application</p>	<p>Do not apply to eyes, mouth or inside the urethra, vagina or anus. No mention of contraindication in pregnancy but Pregnancy category C Difficult for patients to assess maximum dose</p>

Product	Modes of administration	Practical tips	Precautions
Treatment to be applied at the office or in the clinic			
Cryotherapy (liquid nitrogen, CO ₂ , Histofreeze™ or NO ₂)	Apply until a frozen rim of 1-2 mm around the lesion	For exophytic warts, during pregnancy and on mucosa where podophyllotoxin and imiquimod are contraindicated	Can leave painful scars if applied too severely
Bi- or tri-chloroacetic acid 50-80 % in 70 % ethanol	Apply weekly for 6–8 weeks	Washing off is not necessary	Can leave painful scars if applied too severely
Electro-fulguration, CO ₂ laser or surgical ablation	Under local or general anesthesia For major lesions of the genital, perineal or anal area	Residual pain or scarring possible	Can leave painful scars if applied too severely
Podophylline 25 % (Podofilm™)	Apply once or twice a week No more than 1-2 mL per visit. Wash off 1-4 hours after application	Should not be used unless other options not available	Do not apply to uterine cervix, meatus, vagina or in the anus. Contraindicated during pregnancy

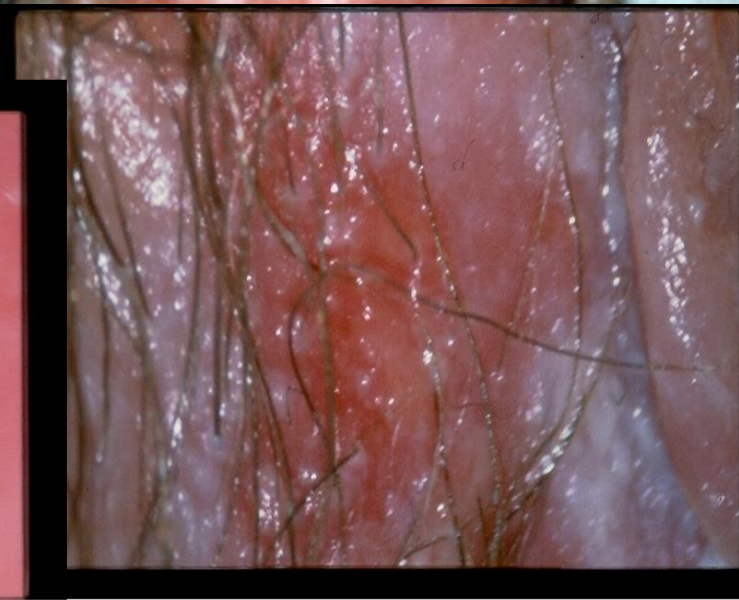


Treatment Options According to Wart Location¹

Treatment	Wart Location				
	Intra vaginal	Cervix	Urethral meatus	Intra-anal	Oral
Surgical removal	☐	☐	☐	☐	☐
Cryotherapy	☐	☐	☐	☐	☐
Electrosurgery	☐	☐	X	☐	☐
Trichloroacetic acid	☐	☐	☐	☐	☐
Imiquimod	X	X	☐	X	X
Podophyllotoxin	X	X	☐	X	X
Laser	☐	☐	☐	☐	☐

1. Adapted from: Prendiville W, Davies P, eds. London, UK. *The Health Professional's HPV Handbook*. ECCCE; Taylor & Francis; 2004.

All treatment options have side-effects



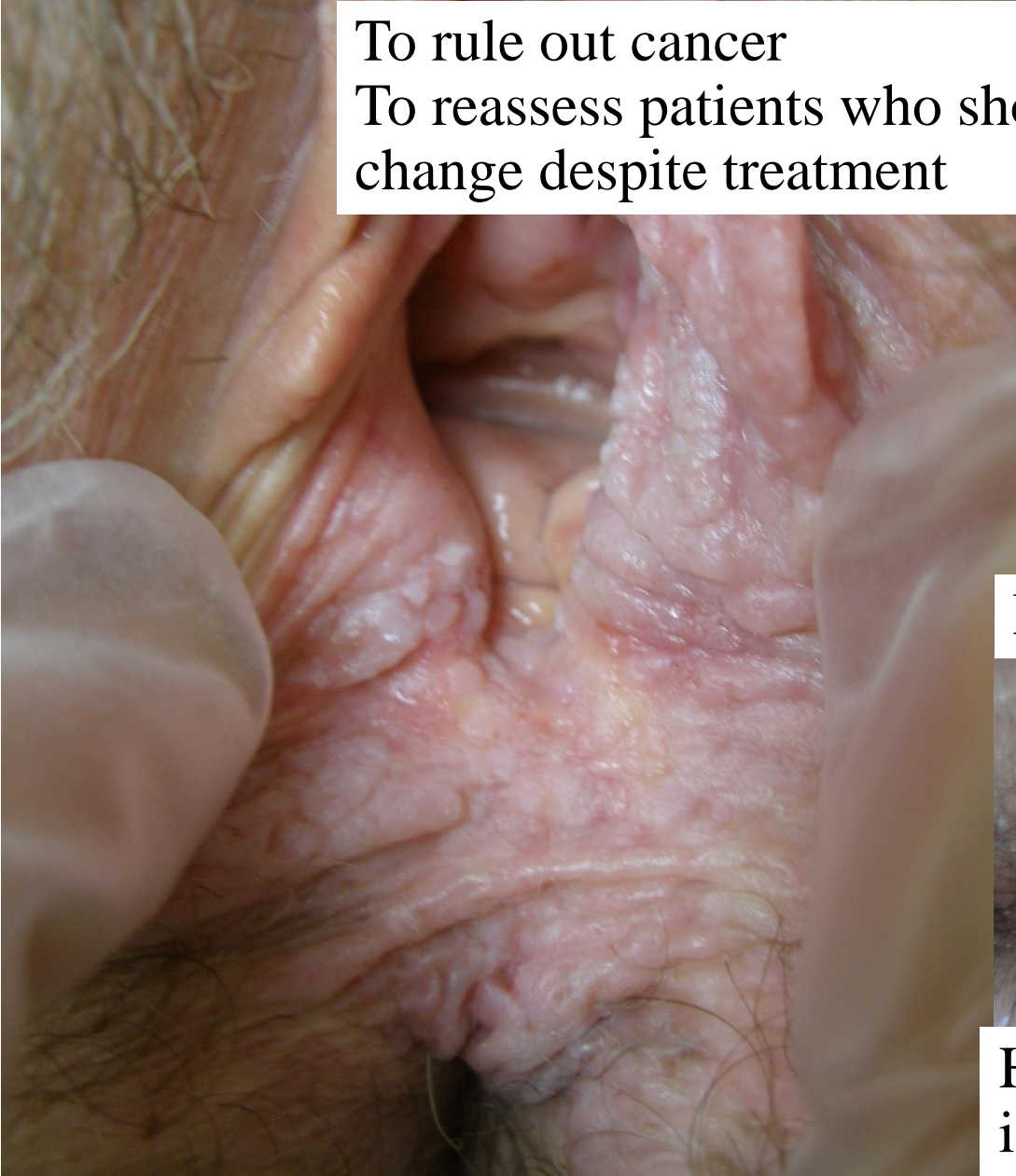
Need for colposcopy or high resolution anoscopy?

- HPV is a multifocal infection
- Higher risk for CIN
- Higher risk for anal cancer if had anal wart treatment

Men	# with anal cancer	# expected	SIR	CI-95% Superior	CI-95% Inferior
Sex					
Women	4	0,054	73,5	19,1	163,2
	11	0,084	130,7	64,9	219,4
Region					
Montréal	14	0,064	217,4	118,4	346,1
Other regions	1	0,066	15,2	0,0	59,8
Total	15	0,139	107,7	60,1	169,1

When to refer to an experienced colleague?

To rule out cancer
To reassess patients who show no change despite treatment

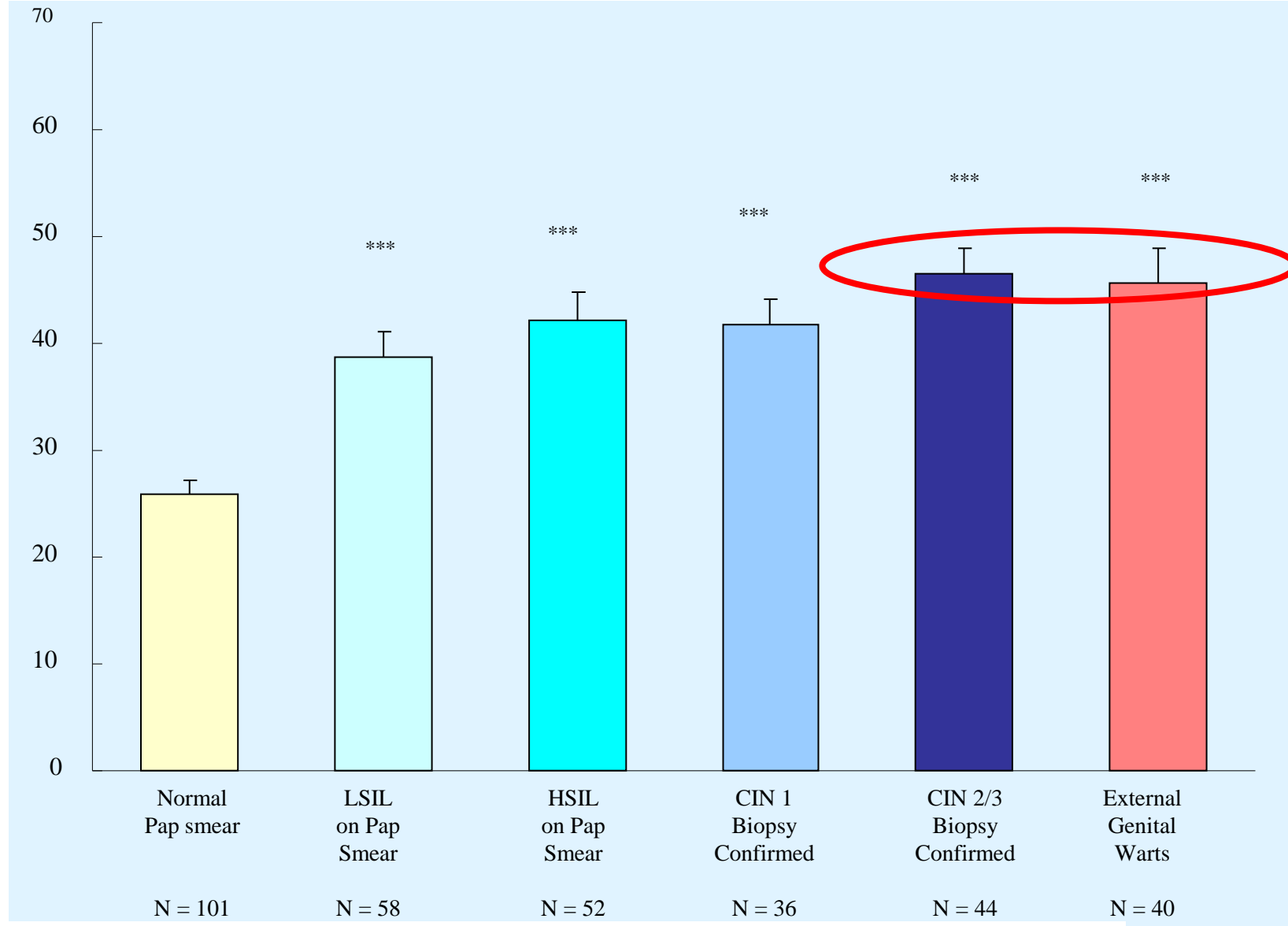


Massive lesions



HIV+ patients to optimize or initiate HAART

The psychosocial burden of HPV-related disease: Overall HIP [HPV Impact Profile] scores by study group



Pirotta MV, Ung L, Stein AN, Conway L, Fairley CK, Garland SM. STI 2009:



I am against
all wart
vaccines!

Thank you for your attention!

Presenter



Dr. R. Jun Lin, MD, FRCSC, MSc

Assistant Professor, Temerty Faculty of Medicine,
University of Toronto

Department of Otolaryngology-Head & Neck Surgery
Head, Division of Laryngology

Unity Health Toronto – St. Michael's Hospital
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Low-Risk HPV Disease in the Larynx: Recurrent Respiratory Papillomatosis

R. Jun Lin, MD, FRCSC, MSc

Assistant Professor

Head, Division of Laryngology

Department of Otolaryngology - HNS

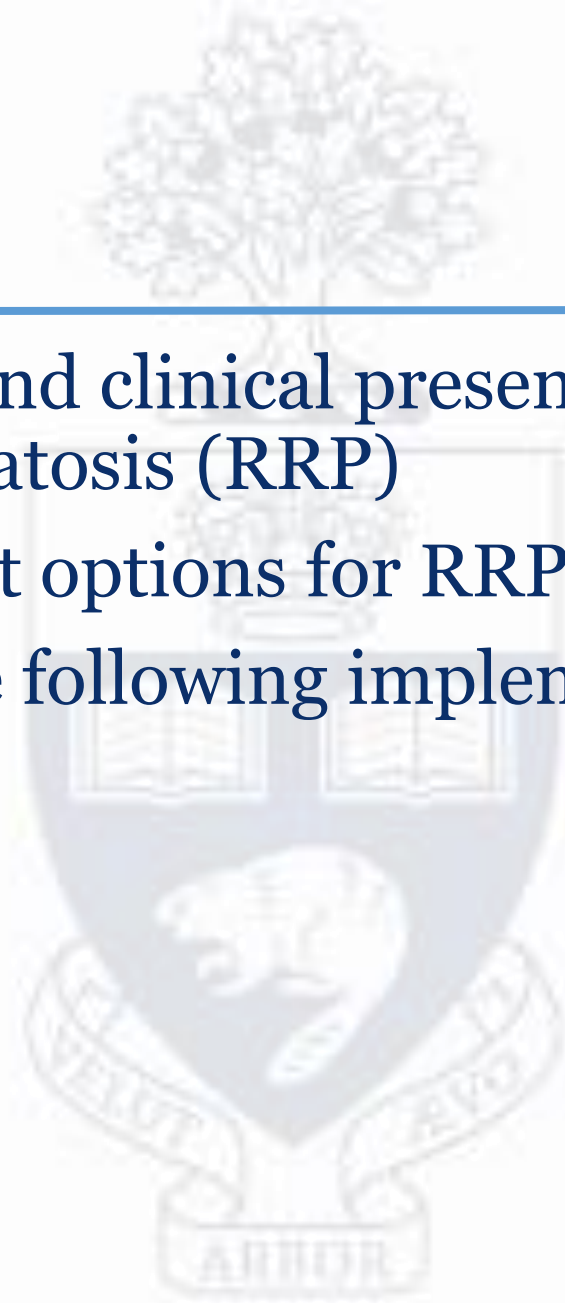
Temerty School of Medicine, University of Toronto

Sep 13, 2023



Objectives

- Summarize etiology and clinical presentation of Recurrent Respiratory Papillomatosis (RRP)
- Understand treatment options for RRP
- Review incidence rate following implementation of HPV vaccination program



Disclosure

- None to declare
- Research supported by
 - Department of OHNS, University of Toronto
 - American Laryngological Association
 - Academic Medical Organization of Southwestern Ontario



What is RRP?

- A rare disease
 - 1.8-5.4 per 1,000,000 in adults
 - 1.7-13.4 per 1,000,000 in children
- Most common benign neoplasm of the larynx
- Cause by low-risk human papillomavirus (HPV) types
 - HPV 6 & 11
- Larynx is the most commonly affected site
 - True vocal folds
 - Supraglottis



Clinical presentation

- Bimodal to trimodal of peak presentation
 - Age 2-7
 - Age 35-45
 - >64
- Two clinical types
 - Juvenile-onset (JoRRP, \leq age 12)
 - May be acquired during birth from infected genital tract
 - Cesarean section does not prevent transmission
 - Equal male and female distribution
 - Adult-onset (AoRRP, $>$ age 12)
 - Sexually transmitted
 - More common in men (3:1)
 - Burden of disease similar between the two sexes

Sex Differences in Oral HPV Infection

- 5-fold higher oral HPV 16 prevalence observed in US men

Lifetime oral
& vaginal
sexual
partners

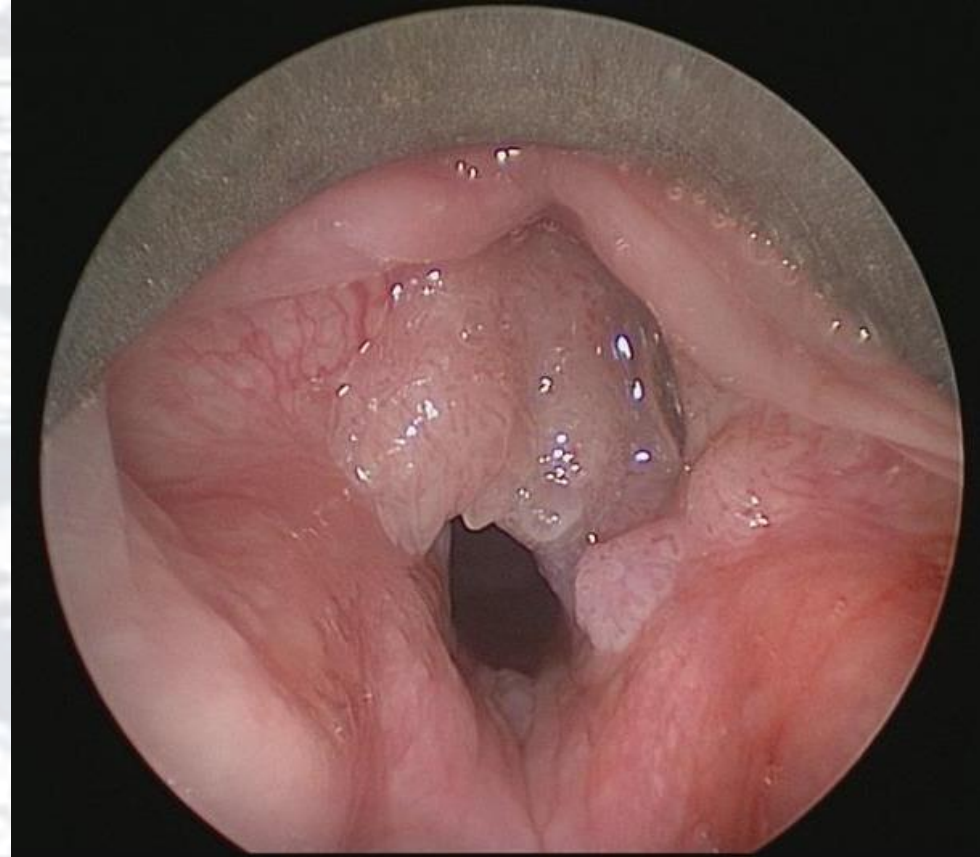
Recent
heterosexual
oral sex
partners

Lower
infection
clearance

D'Souza et al. PLOS ONE. 2014.
D'Souza *et al.* JID. 2016.
Chaturvedi et al. Cancer Res. 2015.

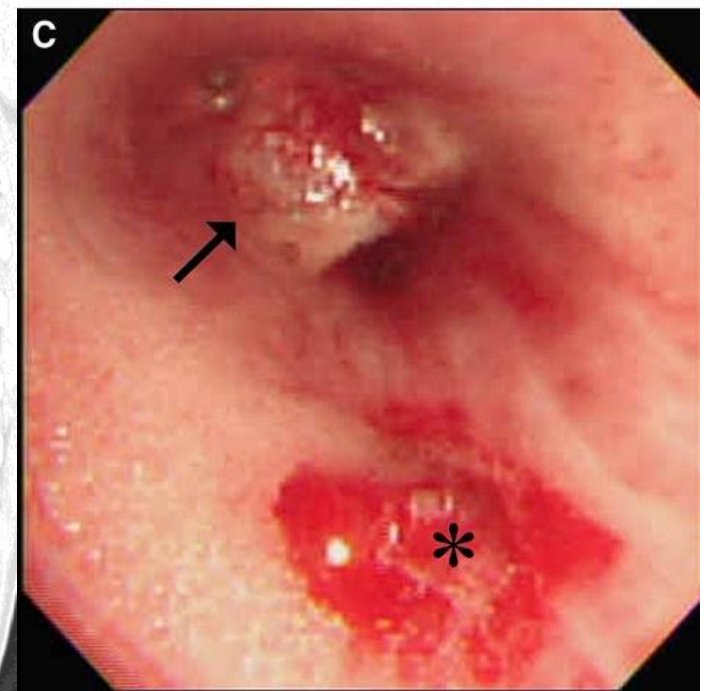
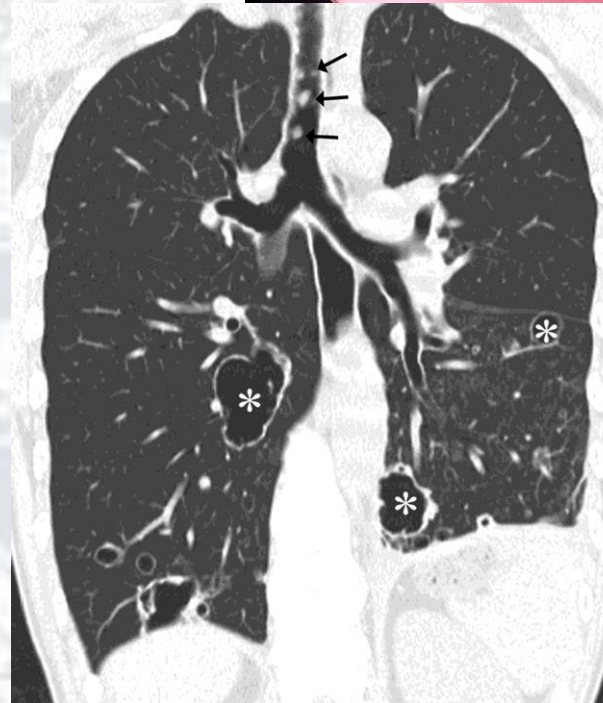
Clinical presentation

- JoRRP
 - Stridor
 - Respiratory distress
 - Dysphonia
- AoRRP
 - Dysphonia
 - Rarely dyspnea



Sequelae of RRP

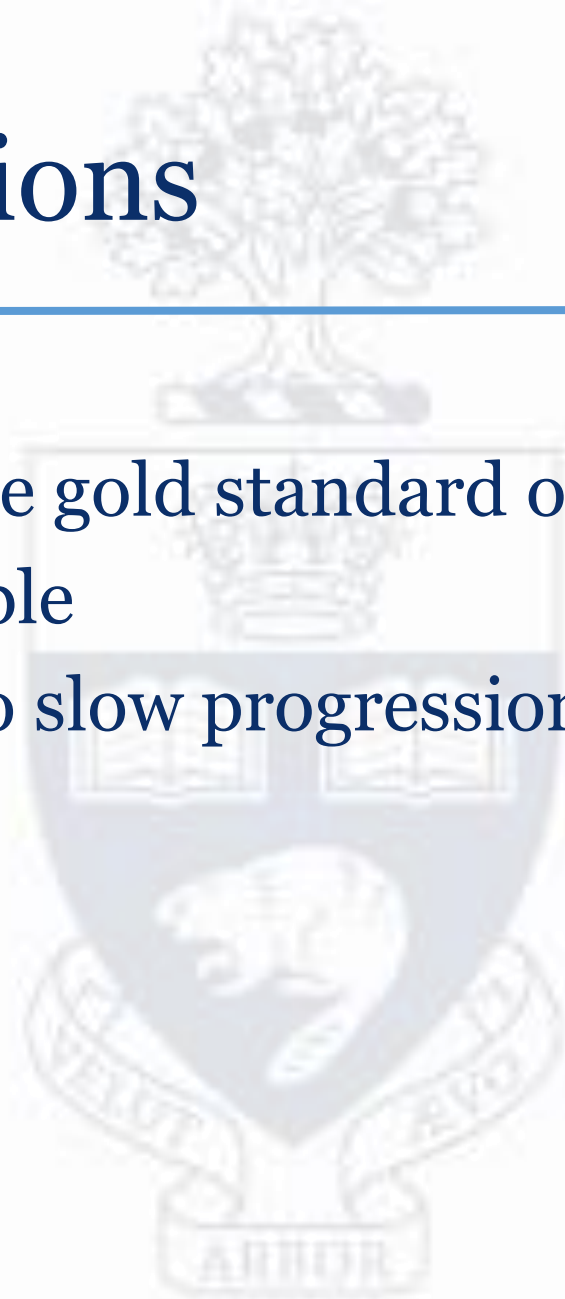
- Permanent dysphonia
 - Glottic scarring
- Extralaryngeal spread
 - Trachea
 - Bronchi & lung
- Malignant degeneration



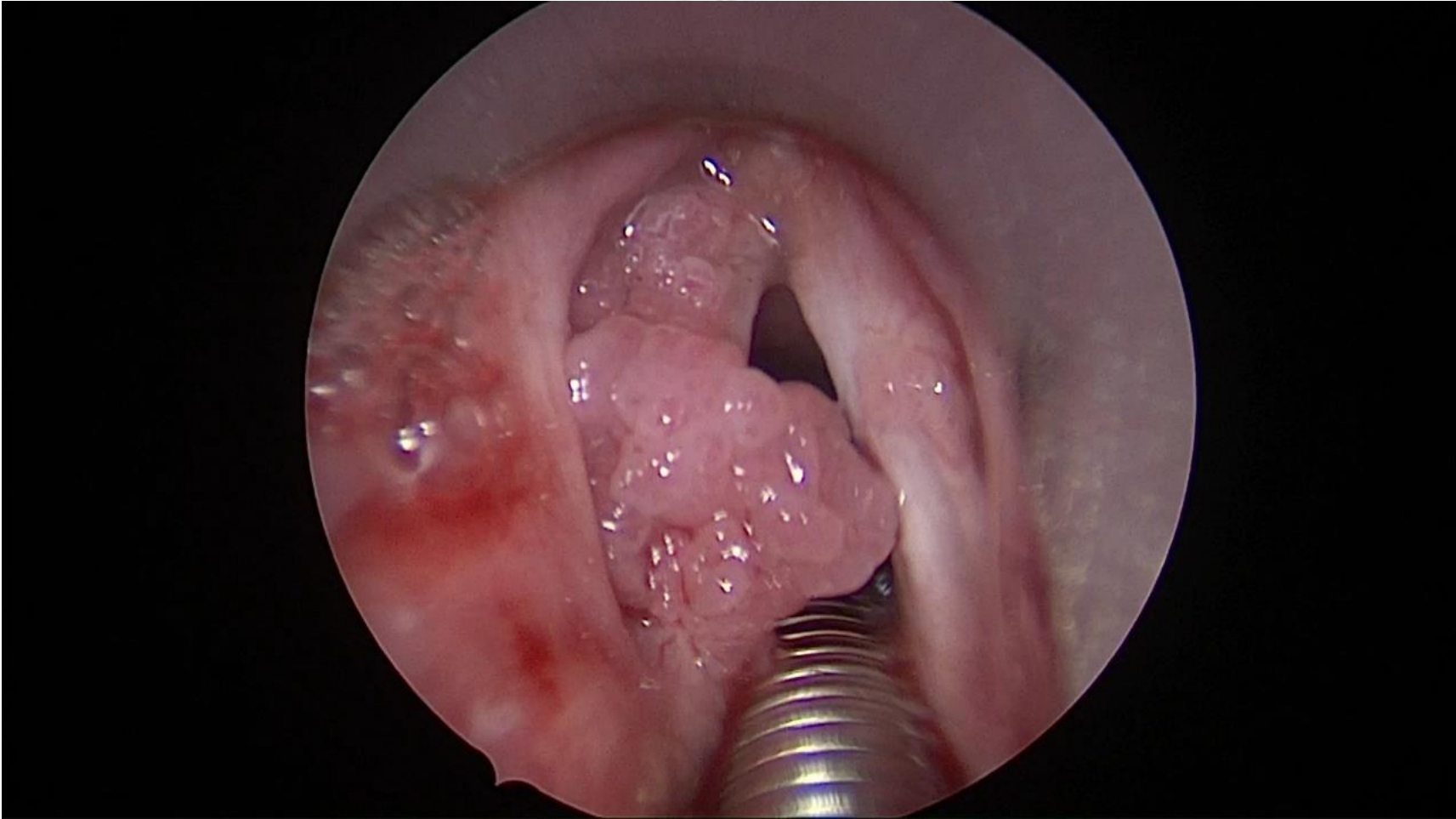
Shiau *et al.* BMJ. 2014

Treatment options

- No cure exists
- Surgical removal is the gold standard of treatment
- Recurrence is inevitable
- Adjuvant treatment to slow progression & recurrence



OR surgical excision



In-office “touch up” treatment



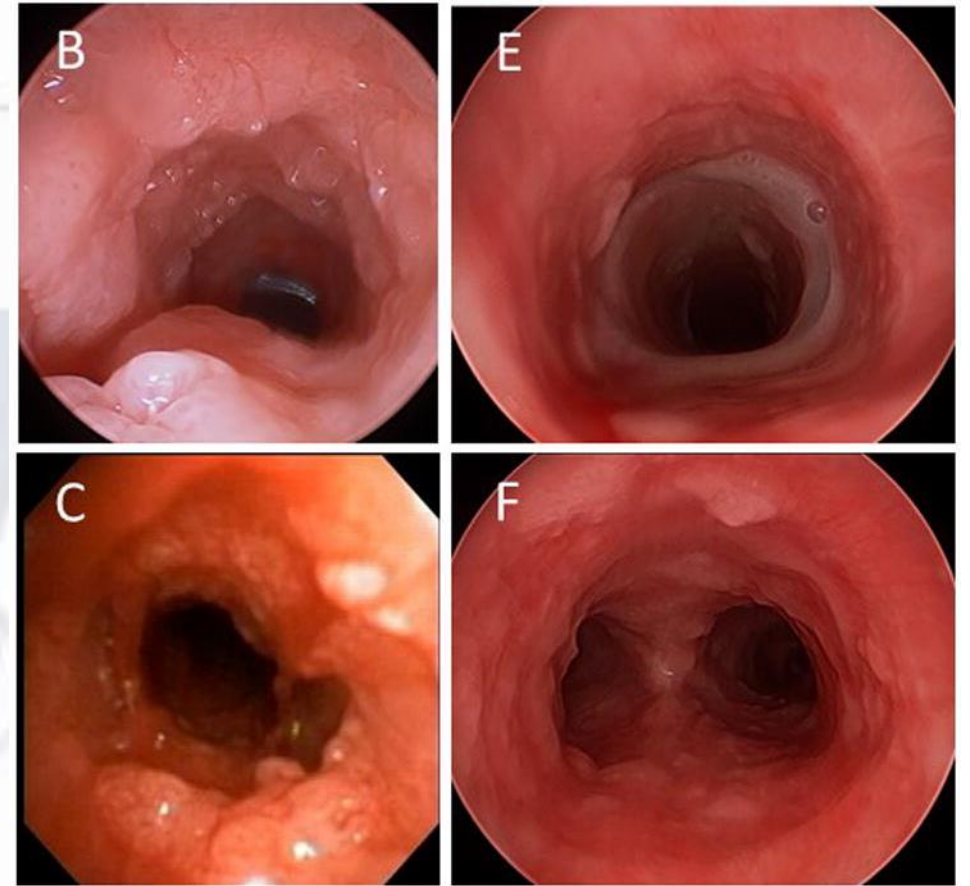
Inter-surgical interval varies

- Frequency of treatment varies individually
 - “Playing catch up”
 - Followed by a quiescent phase
 - Some do require regular interventions
 - Typically life-long follow-up



Adjuvant treatment options

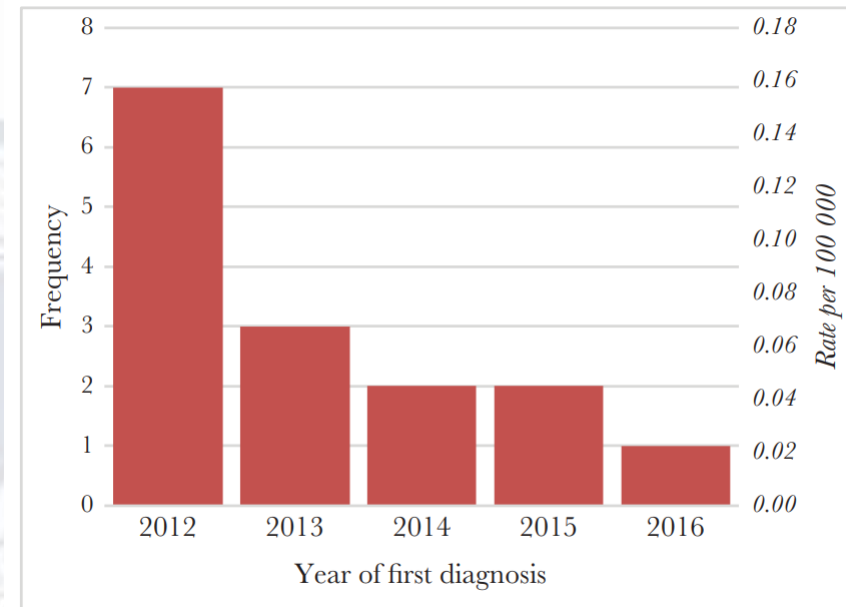
- Indole-3-carbinol (I3C) supplement
- Cidofovir injections
- Bevacizumab (Avastin) injections
- IV Avastin
- Clinical trial (eg. PD-L1 inhibitors)



Best *et al.* Laryngoscope. 2017

Vaccination reduces JoRRP incidence

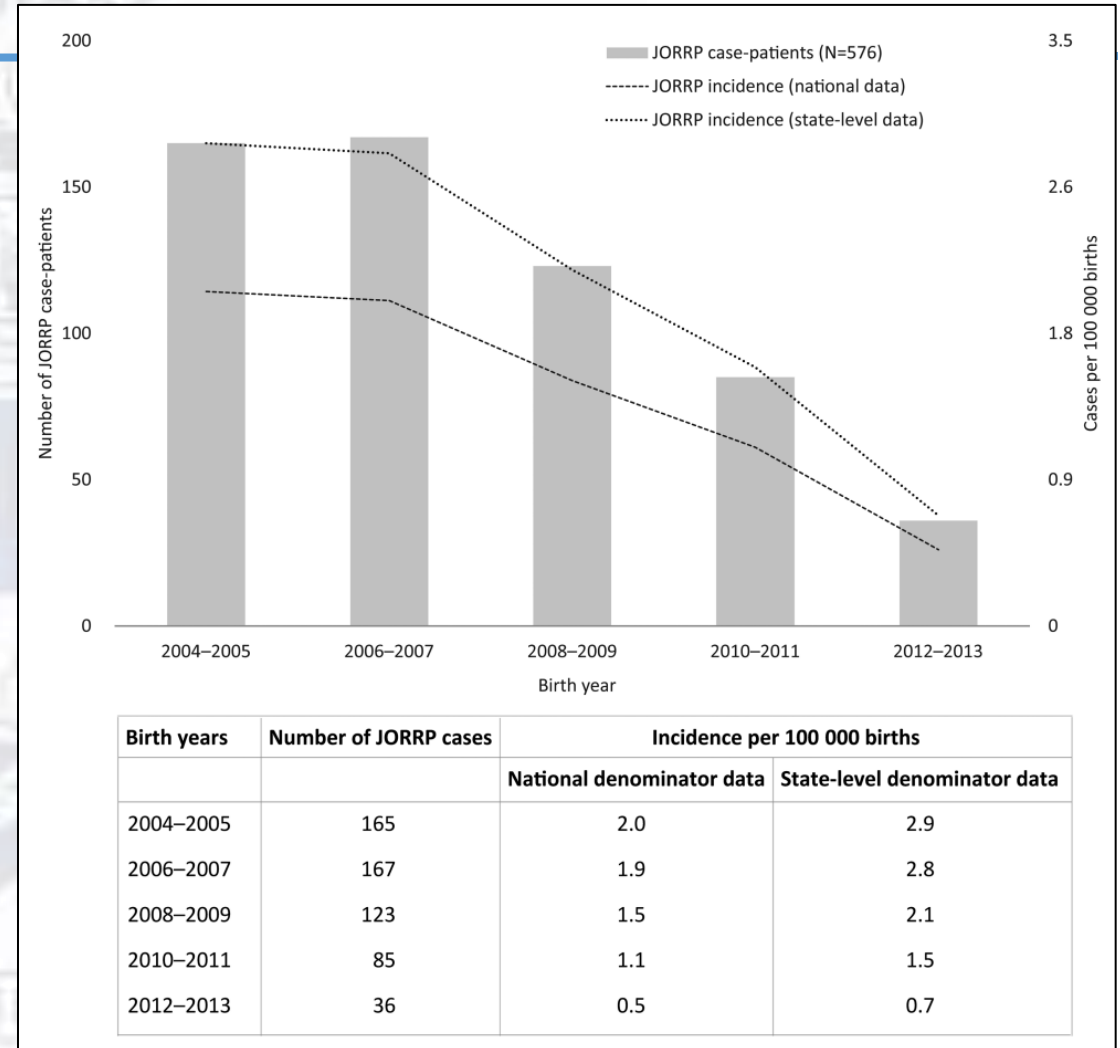
- Australian national HPV vaccination program 2007
 - Quadrivalent Gardasil (6, 11, 16, 18)
 - Available to girls & boys aged 12-13
 - Annual incidence rates declined
 - 1.6/1,000,000 in 2012
 - 0.2/1,000,000 in 2016



Novakovic *et al.* JID. 2018

Vaccination reduces JoRRP incidence

- In the US, Gardasil was introduced in 2006
- Similar reduction in JORRP incidence was observed
- By 2019, aged 13-17 fully vaccinated in
 - 56.8% female
 - 51.8% male



Summary

- RRP is a serious disease that can be debilitating to patients and their families
- Currently there are no curative treatment and repeat surgical removal is required
- Over the past decade, numbers of JoRRP cases declined significantly
 - Most likely due to HPV vaccination
 - Increasing vaccination uptake could lead to elimination of this HPV-related disease



Thank you

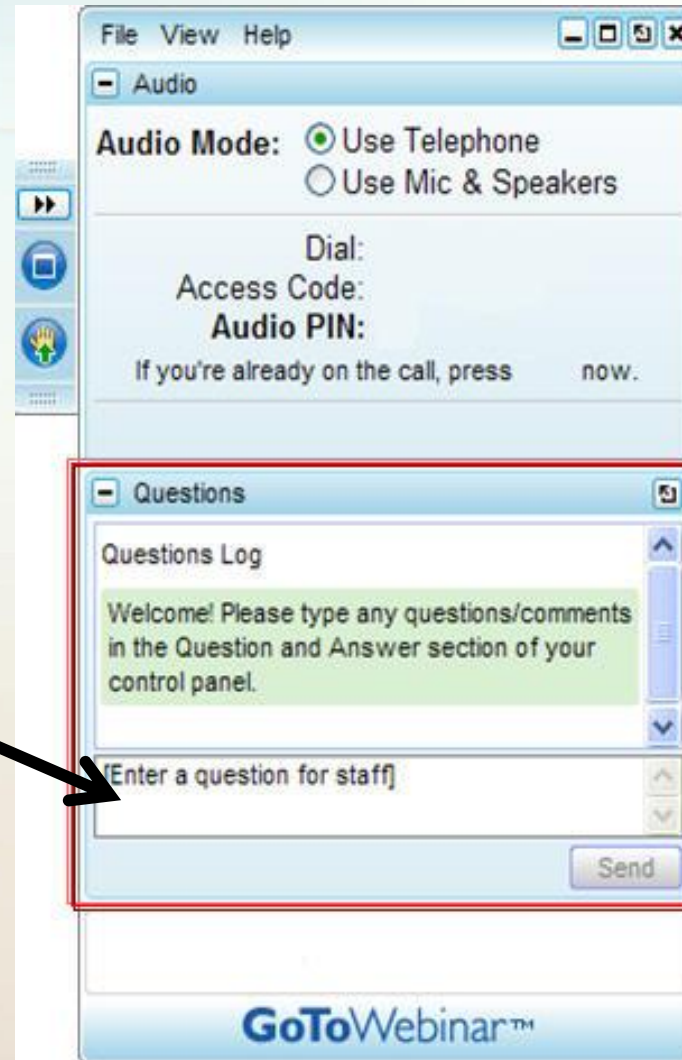
rjun.lin@unityhealth.to



Question & Answer Period

On a computer, submit your text question using the Questions pane

NOTE: On a mobile device, tap on the “?” or “Questions” to open the questions pane



Low-Risk HPV is NOT No-Risk HPV: Anogenital Warts and Respiratory Papillomatosis in Males

Evaluation: https://bit.ly/Low_risk_HPV

Slide Set, Video recording, HPV documents at: www.CIDCgroup.org

Thank you for participating!

This educational program is made possible through the support of **Merck Canada**
The opinions expressed in this webinar are those of the presenter and do not necessarily reflect the views of CIDC or its partners

Next CME webinar: **Pneumococcal Vaccines** – October 25, 2023

Register at: **Bit.ly/Pneumo_Vaccines**

(this link is case-sensitive, so please capitalize **Pneumo** and **Vaccines**)

www.CIDCgroup.org