



Consortium for Infectious Disease Control

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providing continuing medical education, coordinating initiatives, and undertaking research*

Winnipeg, Manitoba, Canada

June 30, 2020

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HPV Prevention in the Adult Population: protecting those at higher risk



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This educational program is made possible through the support of **Merck Canada Inc.**

and with assistance by BD Diagnostics and Immunize Canada

The opinions expressed in this webinar are those of the presenter and do not necessarily reflect the views of CIDC or its partners

Webinar Objectives



- Identify adults at higher risk for HPV infection and disease
- Describe the burden of HPV disease in adult females and males
- State the evidence for HPV vaccination of adult females and males, including vaccination during treatment for HPV-related disease

Housekeeping

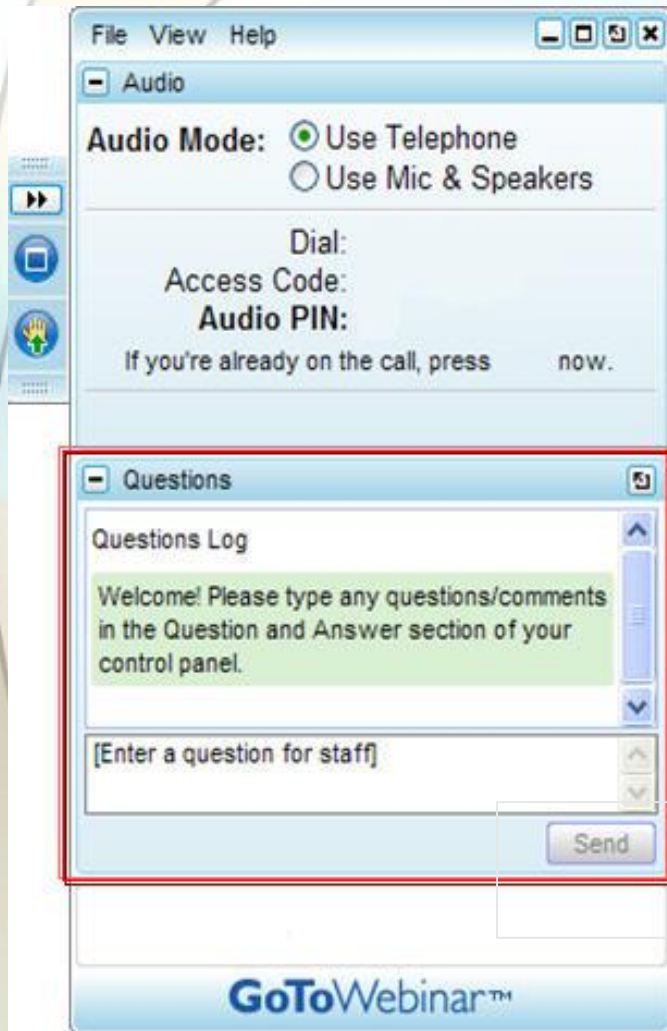


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Moderator



Dr. Marc Steben, MD

- Chair, Canadian HPV Prevention Network
- Family Physician, Family Medicine Group La Cité du Parc Lafontaine
- Board member, International Papillomavirus Society
- Montreal, Quebec, Canada

Presenter



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- **Sunnybrook Health Sciences Centre**
- **Associate Professor, Dept of Obstetrics and Gynaecology**
University of Toronto

HPV Prevention in the Adult Population:

protecting those at higher risk



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Presenter Disclosure

Presenter:

Dr Nancy Durand

Speakers Bureau/Honoraria:

Merck Canada, Merck MSD Global

Consulting Fees:

Merck Canada, Merck MSD Global

Other:

Associate Professor,

University of Toronto

Dept of Obstetrics and Gynaecology

Objectives:

- Identify those at higher and highest risk for HPV infection and disease
- Describe the burden of HPV disease in adult females and males
- Discuss the evidence for HPV vaccination:
 - High risk MSM, HIV+
 - Adult females and males
 - Patients with HPV-related disease

Who is at higher risk?

Higher Risk

- Age
- Males
- MSM
- Past or current history HPV infection/disease

Highest Risk: immune status

- HIV/AIDS
- Immunosuppressive rx, biologics:
 - Autoimmune disorders:
 - SLE, RA, IBD, MS, psoriasis
 - Transplant patients:
 - stem cell, bone marrow,
 - solid organ (kidney, liver, pancreas, heart, lung)

Highest Risk: immune status

- Increased:
 - Prevalence of HPV
 - Prevalence of high-risk types HPV
 - Multiple HPV types
 - HPV viral loads
 - Persistence of HPV
 - Reinfection with HPV
 - Reactivation of latent infection

1. Garland SM, Brotherton JML, Moscicki AB, Kaufmann AM, Stanley M, Bhatla N, Sankaranarayanan R, Sanjose, S, Palefsky, J. HPV Vaccination of immunocompromised hosts. *Papillomavirus Research* 2017; 4:35-38.
2. Segal JP et al. The incidence and prevalence of HPV cancers in IBD. *Inflamm Bowel Disease* Feb 2020. <https://doi.org/10.1093/ibd/izaa035>
3. Furer V, Rondaan C, Heijstek M, et al. Incidence and prevalence of vaccine preventable infections in adult patients with autoimmune inflammatory rheumatic diseases (AIIRD): a systemic literature review informing the 2019 update of the EULAR recommendations for vaccination in adult patients with AIIRD. *RMD Open* 2019;5:e001041. doi:10.1136/rmdopen-2019-001041.
4. Wadström, H. et al. Do RA or TNF inhibitors increase the risk of cervical neoplasia or of recurrence of previous neoplasia? A nationwide study from Sweden. *Ann Rheum Dis*. 2016 Jul;75(7):1272-8. doi: 10.1136/annrheumdis-2015-208263.
5. Grulich A et al. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. *Lancet*. 2007 Jul; 370: 59-67.

Highest Risk: immune status

(RA, IBD, transplant, HIV)

- Increased rates:
 - Cervical HSIL, invasive cancer
 - Vulvar HSIL
 - Anal HG-AIN, anal cancer

Increased rates both with disease and with immunosuppressive Rx

1. Garland SM, Brotherton JML, Moscicki AB, Kaufmann AM, Stanley M, Bhatla N, Sankaranarayanan R, Sanjose, S, Palefsky, J. HPV Vaccination of immunocompromised hosts. *Papillomavirus Research* 2017; 4:35-38.
2. Segal JP et al. The incidence and prevalence of HPV cancers in IBD. *Inflamm Bowel Disease* Feb 2020. <https://doi.org/10.1093/ibd/izaa035>
3. Furer V, Rondaan C, Heijstek M, et al. Incidence and prevalence of vaccine preventable infections in adult patients with autoimmune inflammatory rheumatic diseases (AIIRD): a systemic literature review informing the 2019 update of the EULAR recommendations for vaccination in adult patients with AIIRD. *RMD Open* 2019;5:e001041. doi:10.1136/rmdopen-2019-001041.
4. Wadström, H. et al. Do RA or TNF inhibitors increase the risk of cervical neoplasia or of recurrence of previous neoplasia? A nationwide study from Sweden. *Ann Rheum Dis*. 2016 Jul;75(7):1272-8. doi: 10.1136/annrheumdis-2015-208263.
5. Grulich A et al. Incidence of cancers in people with HIV/AIDS compared with immunosuppressed transplant recipients: a meta-analysis. *Lancet*. 2007 Jul; 370: 59-67.

Highest Risk: immune status

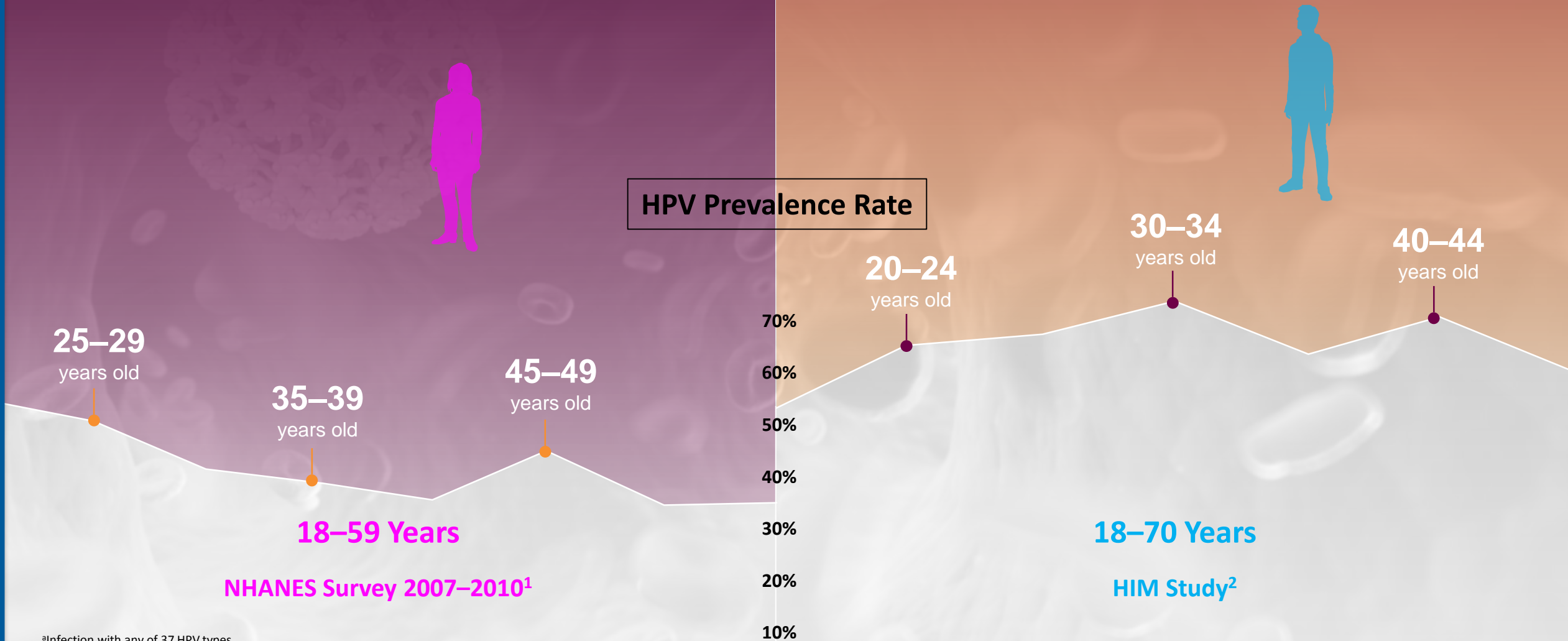
- HIV +
 - HAART (highly active antiretroviral therapy):
 - Modest or no effect on HPV carriage, clearance or persistence
 - Management guidelines on HAART with HIV suppression same as for healthy patients
 - Higher resistance to Rx for EGW

Burden of Disease

Adult females

Adult males

HPV Infection Is Common Among Adults^a



^aInfection with any of 37 HPV types.

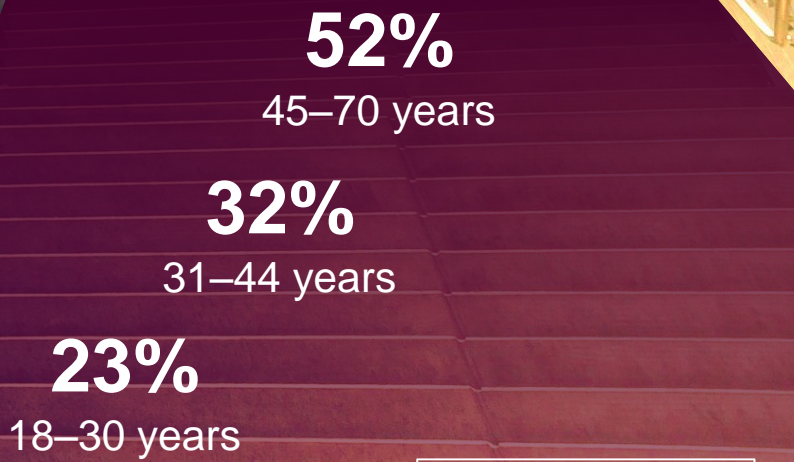
NHANES = National Health and Nutrition Examination Survey; HIM = Human Papillomavirus Infection in Men study.

1. Shi R et al. *BMC Res Notes*. 2014;7:544. 2. Giuliano AR et al. *Cancer Epidemiol Biomarkers Prev*. 2008;17:2036–2043.

Persistent HPV Infection Increases With Age^{1,2,a}



Costa Rica study



^aPersistent infection with any of 37 HPV types in males and >40 types in females.^{1,2}
1. Nyitray AG et al. *J Infect Dis.* 2011;204:1711–1722. 2. Castle PE et al. *J Infect Dis.* 2005;191:1808–1816.

HIM study

Burden of HPV-Related Disease in Males Is Increasing

Genital warts
Recurrent respiratory papillomatosis

>90% caused by
HPV 6 and 11^{1,2}

Anal cancer 
Penile cancer 
Oropharyngeal and oral cavity cancers 

≈30%–90% caused by
HPV 16 and 18^{3–5}

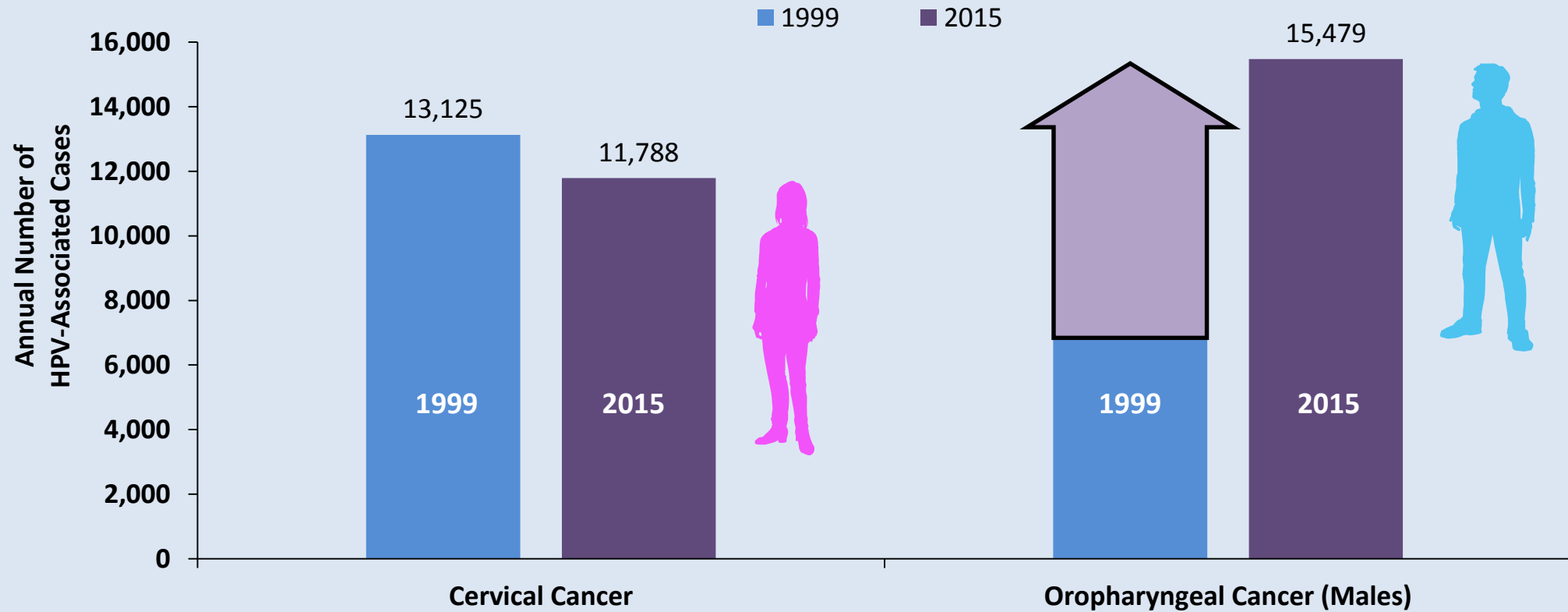
There are no routinely available, recommended screening methods for cancers caused by HPV in men

None of the available HPV vaccines are indicated to prevent oropharyngeal cancer, penile cancer, or recurrent respiratory papillomatosis.

HPV = human papillomavirus.

1. Greer CE et al. *J Clin Microbiol.* 1995;33:2058–2063. 2. Freed GL et al. *Int J Pediatr Otorhinolaryngol.* 2006;70:1799–1803. 3. De Vuyst H et al. *Int J Cancer.* 2009;124:1626–1636. 4. Miralles-Guri C et al. *J Clin Pathol.* 2009;62:870–878. 5. Kreimer AR et al. *Cancer Epidemiol Biomarkers Prev.* 2005;14:467–475.

US: Males Diagnosed With HPV-Related Oropharyngeal SCC Doubled Over 15 Years¹

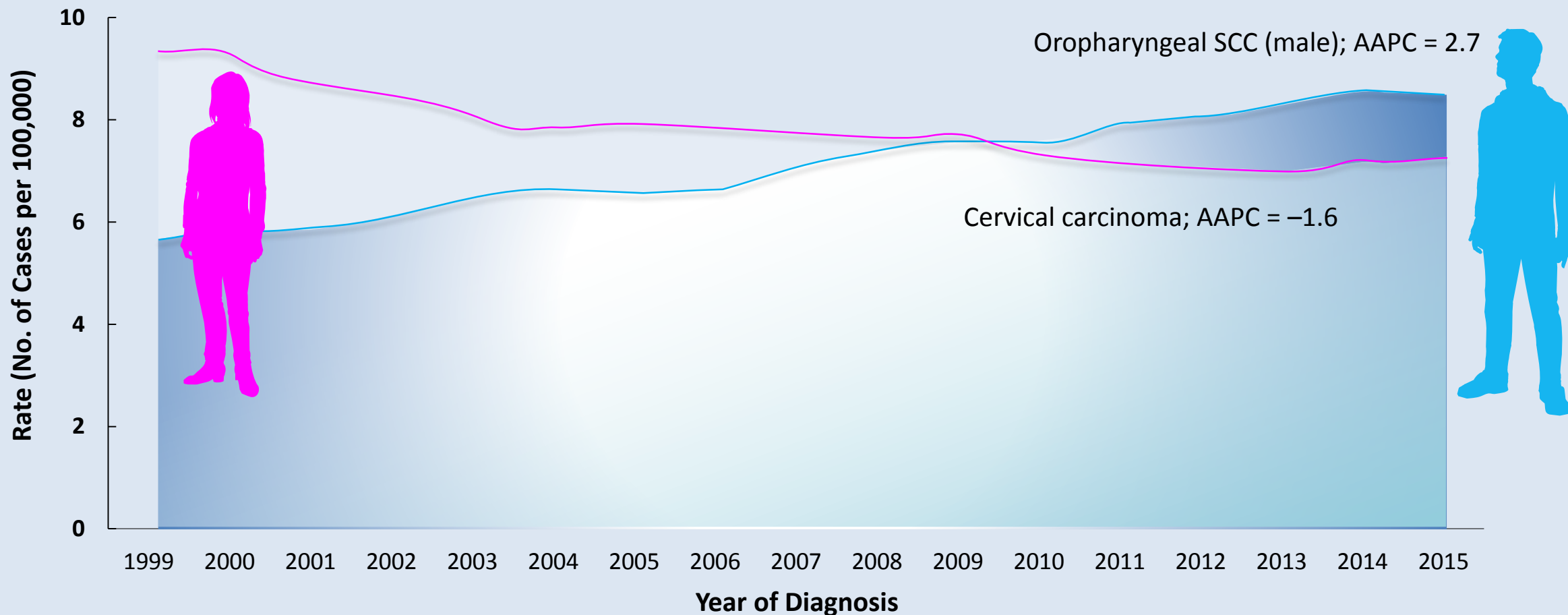


HPV = human papillomavirus; SCC = squamous cell carcinoma.

1. Van Dyne EA et al. *MMWR Morb Mortal Wkly Rep.* 2018;67:918–924.

incidence of OPC in females did not change

US: Rates of Cervical Cancer Are Declining While HPV-Related Oropharyngeal SCC in Males Is Rising¹



HPV = human papillomavirus; SCC = squamous cell carcinoma; AAPC = average annual percent change.

1. Van Dyne EA et al. *MMWR Morb Mortal Wkly Rep.* 2018;67:918–924.

Vaccination of Immunocompromised Hosts

Recommendations

Canadian provincial programs

Recommendations: immunocompromised

- 3 dose schedule (regardless of age)
- Vaccinate as early as possible
- Lower antibody titers
- ❖ Still well above levels seen with natural infection
- Safe; not associated with significant adverse events
- Clinical course of disease was not affected

Publicly Funded HPV Immunization Programs in Canada: (June 2020)



Province/Territory	HPV Vaccination Program	Uptake Rates
British Columbia	9V - females and males Gr. 6 (2 doses) ; HIV + (9-26); high-risk males 9-26, Transgender 9-26, <i>Catch up: Females and males (born in 2006 or later) vaccination initiated before 19 and catch up to 26</i>	66 %
Alberta	9V - females and Males Gr. 5 (2 doses) ; catch up to age 26, Males and Females 17-26, Hematopoietic Stem Cell Transplantation (HSCT) recipients, Solid organ transplant (SOT) candidates and recipients:	66 %
Saskatchewan	9V - females and males Gr. 6 (2 doses) ; HIV+ males (9-17)); HIV+ males (9-17), Catch up: Females born since 1996; Males born since 2006, Females and males younger than 27 years old with specific medical conditions, Publicly Funded Immigrant and Refugee Immunization	61 %
Manitoba	9V -females and males Gr. 6 (2 dose) ; HIV+ and immunocompromised 9-26/9-45; Dx RRP (past or present), Men < 18 incarcerated (past or present), Gay bisexual male & Transgender 9-26, Sexual assault victims male 9-26 & female 9-45, Female 9-45 with new HG-cervical pathology, <i>Catch up: Females: Born 1997 or later; Males: Gr. 8/9 (born 2002 or later.</i>	58 %
Ontario	9V - females and males Gr. 7 (2 doses) ; high-risk males 9-26; catch up until grade 12,; public health sexual health clinics – those with multiple sex partners up to 26	56 %
Quebec	9V / C2- females and males Gr 4 (1 dose 9V; 1 dose C2) ; catch-up females and males <18; immunocompromised men or women (9-26)	76 %
New Brunswick	9V - females and males Gr. 7; (2 doses) ;	75 %
Nova Scotia	9V-females and males Gr. 7; (2 doses) HIV and MSM 9-45	80 %
Prince Edward Island	9V - females and males Gr 6 ; (2 doses) ; high risk males (18-26) and females (18-45), All who missed vaccine in Gr. 6 since 2017	84 %
Newfoundland	9V -females and males Gr 6 (2 doses) ;	88 %
Northwest Territories	9V -females and males Gr. 4 (2 doses) ; catch up males and females 9-26	39 %
Yukon Territory	9V -females and males Gr. 6; (2 doses) ; catch up females age 15-18; Females and Males HIV+ 9 – 45, Males high risk (9–26) ; MSM; Street involved	67 %
Nunavut	9V -females and males Gr. 6 ≥ 9 yrs (2 doses)	--

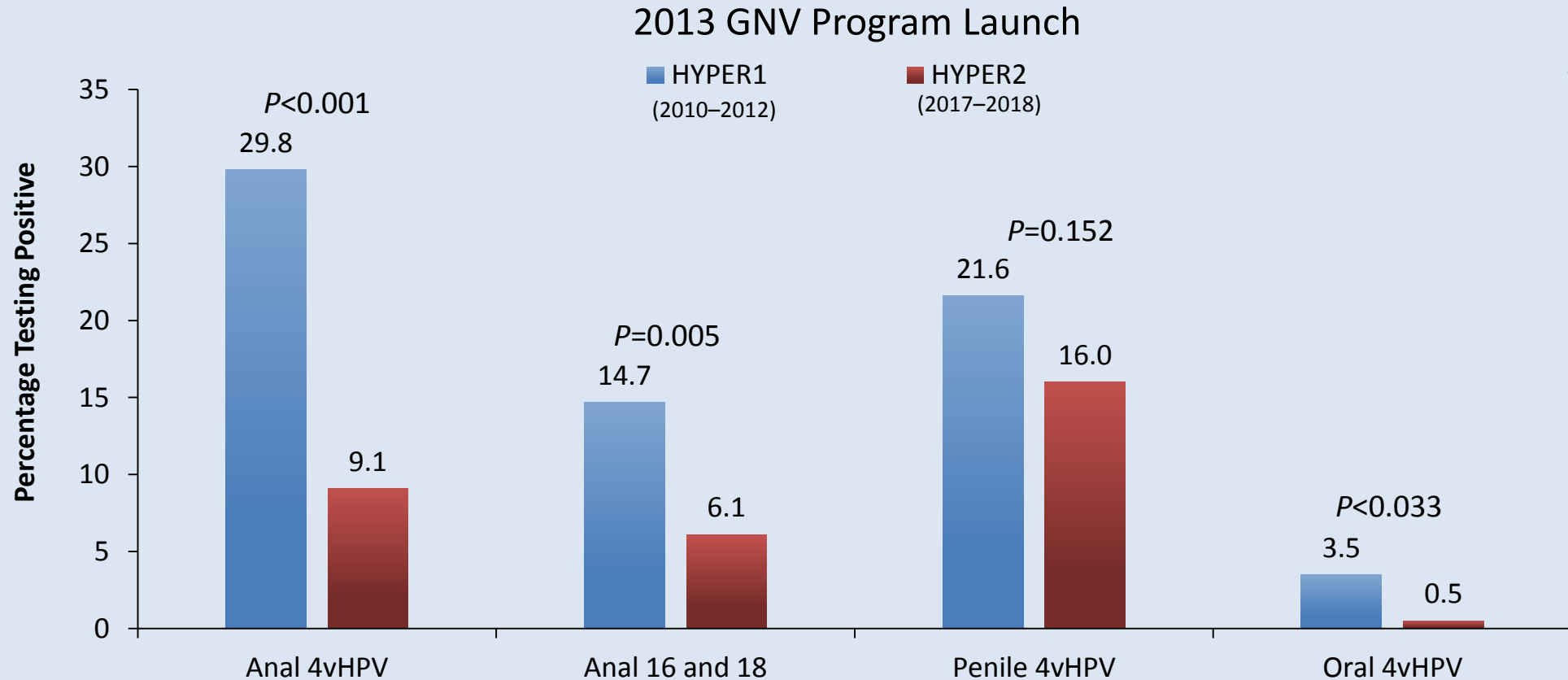
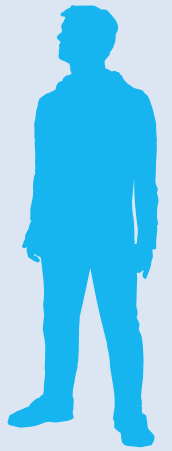
Evidence

4vHPV prevalence in MSM and bisexual males

4vHPV vaccine in HIV +



Australia: HPV Prevalence in High-Risk MSM and Bisexual Males 5 Years After GNV (HYPER2 Study)



School-based vaccination program in females commenced in 2007.

In 2013, the program was extended to include males aged 12–15 years plus a 2-year catch age of <16 years.

HPV = human papillomavirus; MSM = men who have sex with men; GNV = gender-neutral vaccination; 4vHPV = 4-valent human papillomavirus.

1. Zou H et al. *J Infect Dis.* 2013;209:642–651. 2. Chow E et al. *EUROGIN* 2019. Abstract 0147.

4vHPV Vaccine Studies in HIV+

- 4vHPV vaccine in HIV+ girls¹, boys² and adult males³:
 - Immunogenic, although lower levels than HIV-
 - Higher levels than non-vaccinated⁴
 - Safe
- 4vHPV vaccine in HIV+ adult males:
 - Persistent immunity over two years later⁵

1. Mugo, N et al. Quadrivalent HPV vaccine in HIV-1-infected early adolescent girls and boys in Kenya: Month 7 and 12 post vaccine immunogenicity and correlation with immune status. *Vaccine* 36 (2018) 7025–7032
2. Wilkin T, Lee JY, Lensing SY, Stier EA, Goldstone SE, Berry JM, et al. Safety and immunogenicity of the quadrivalent human papillomavirus vaccine in HIV-1-infected men. *J Infect Dis*. 2010; 202(8):1246. <https://doi.org/10.1086/656320> PMID: 20812850
3. Levin MJ, Moscicki AB, Song LY, Fenton T, Meyer WA 3rd, Read JS, et al. Safety and immunogenicity of a quadrivalent human papillomavirus (types 6, 11, 16, and 18) vaccine in HIV-infected children 7 to 12 years old. *J Acquir Immune Defic Syndr*. 2010; 55(2):197. <https://doi.org/10.1097/QAI.0b013e3181de8d26> PMID: 20574412
4. Hidalgo-Tenorio et al. *AIDS Res Ther* (2017) 14:34 DOI 10.1186/s12981-017-0160-0
5. Ellsworth G, Lensing S, Ogilvie C, Lee J, Goldstone S, Berry-Lawhorn J, et al. A delayed dose of quadrivalent human papillomavirus vaccine demonstrates immune memory in HIV-1-infected men. *Papillomavirus Research*. 2018; 6:11–4. <https://doi.org/10.1016/j.pvr.2018.05.001> PMID: 29807211

Evidence

Adult female clinical trials

Adult male clinical trials

LTFU of clinical trials

14-Year Follow-up on the Long-Term Effectiveness of the **4vHPV** Vaccine in Females 16–23 Years of Age



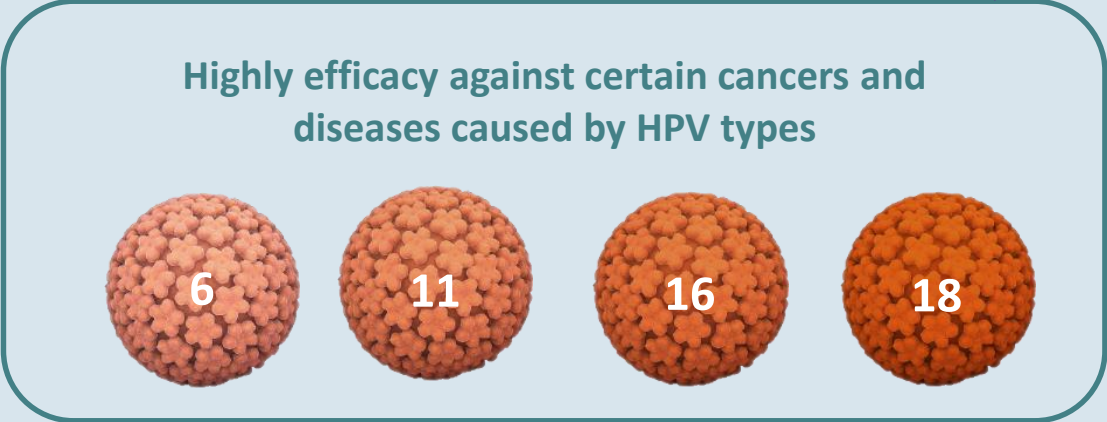
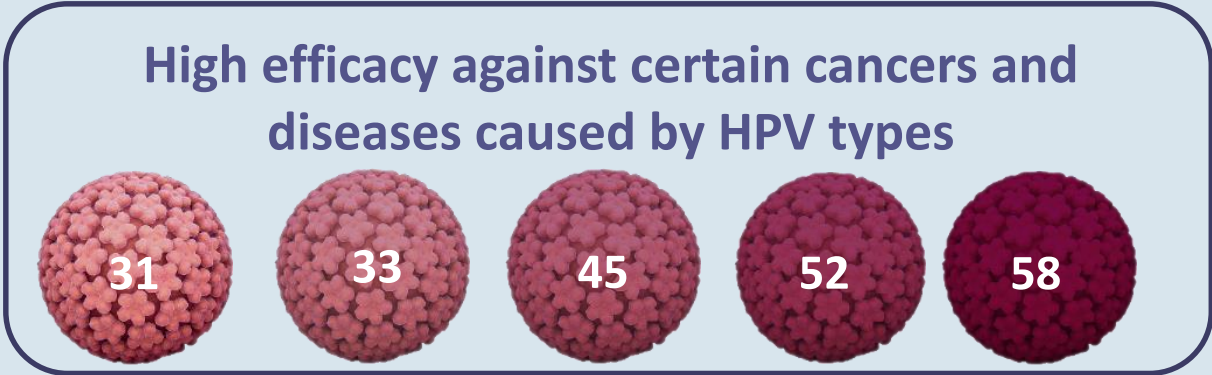
100%
efficacy against CIN2+

14
years

100%
efficacy against cervical, vulvar,
and vaginal cancer

4vHPV = 4-valent human papillomavirus; CIN = cervical intraepithelial neoplasia.
Kjaer SK et al. *Clin Infect Dis*. 2018;66:339–345;
Kjaer SK et al. Presented at EUROGIN 2018, Lisbon, Portugal. Abstract 00625.

6 years Effectiveness of 9vHPV Vaccine in Females aged 16-26¹



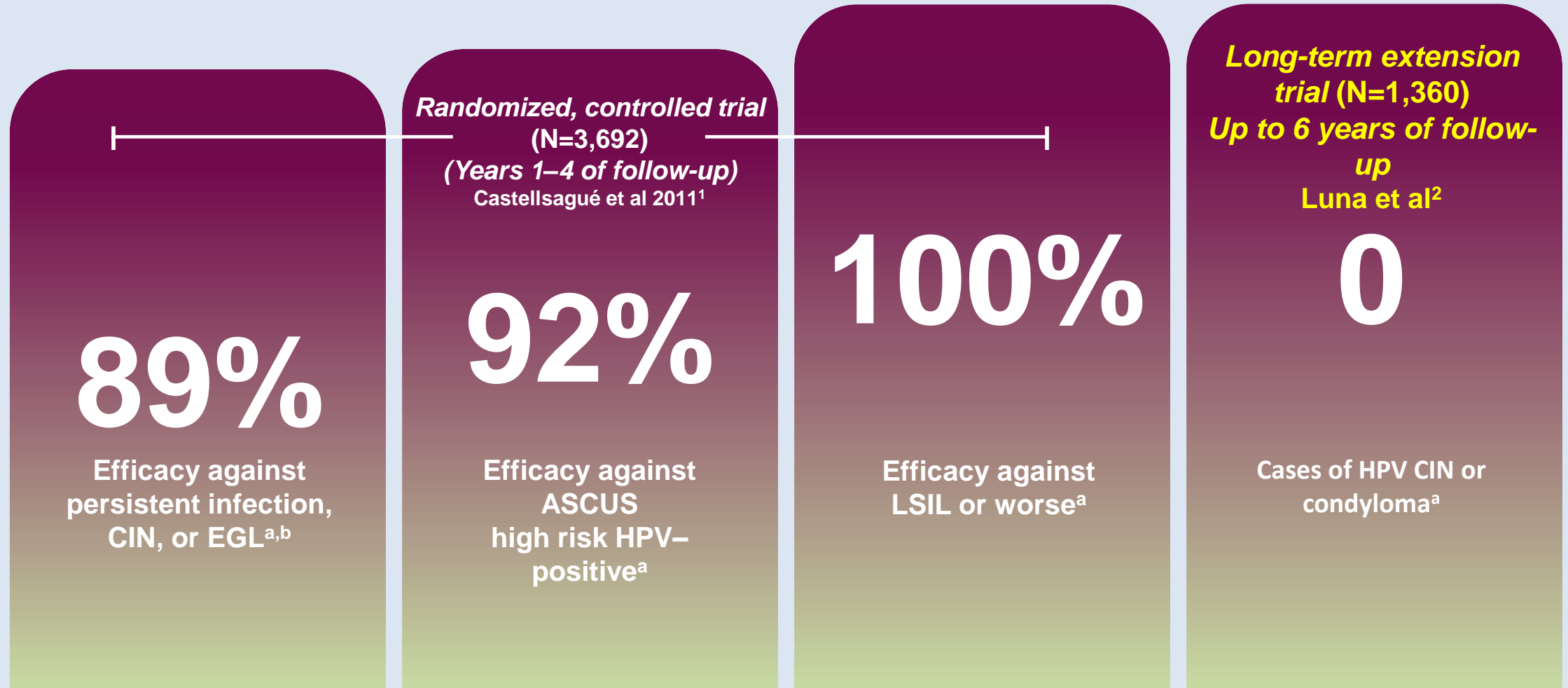
High-grade cervical, vulvar, or vaginal disease

Cervical cancer, CIN2/3, or AIS

Persistent infection at 12 months

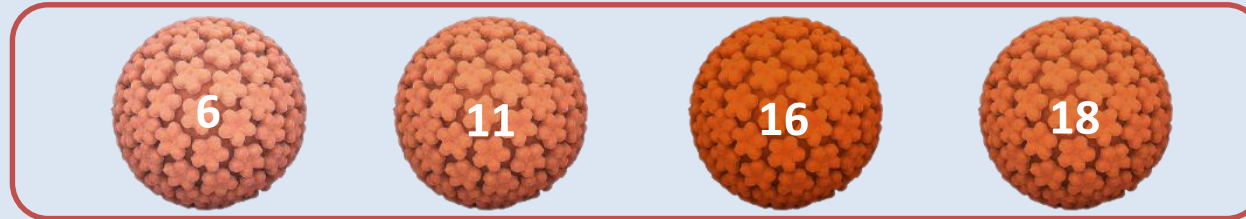
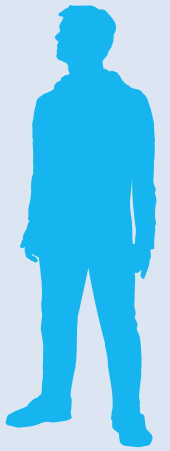
CIN = cervical intraepithelial neoplasia; AIS = adenocarcinoma in situ.
1. Huh WK et al. *Lancet*. 2017;390:2143–2159. 2. Data up to 8 years presented at Eurogin 2019

Quadrivalent Future III - **Mid-Adult Women Trial**^{1,2} (females age 24-45)




1. Castellsagué X et al. *Br J Cancer*. 2011;105:28–37. 2. Luna J et al. *PLoS ONE*. 2013;8:e83431.

Efficacy and Effectiveness of the 4vHPV Vaccine in Males 16–26 Years of Age Through 10 Years




90%
reduction in external
genital lesions¹


RCT
Years
1–3


78%
reduction
in AIN^{2,a}


0
cases of EGL³


LTFU
Years
4–10

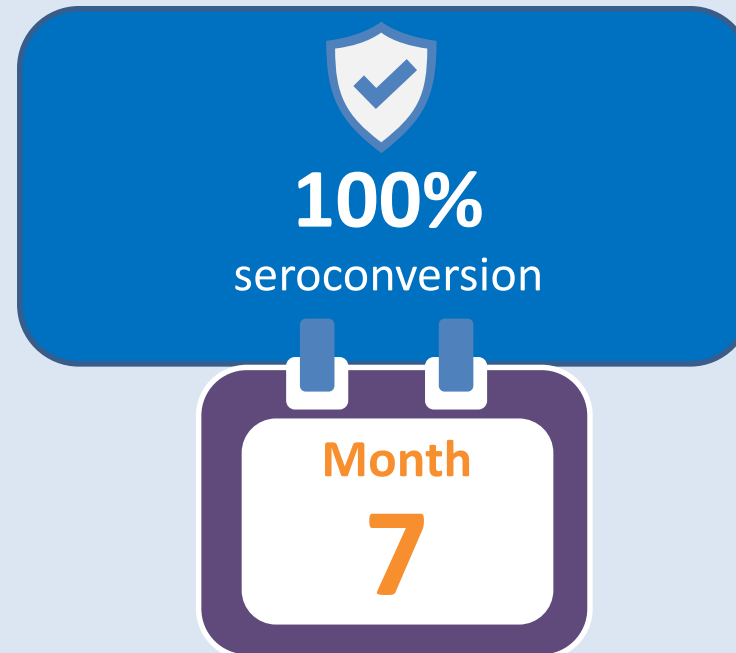
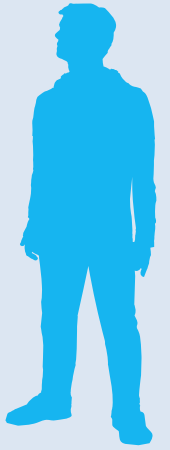

0
cases AIN2/3^{3,a}

Males aged 16–26 years; ^aMSM subset.

AIN = anal intraepithelial neoplasia; EGL = external genital lesions; LTFU = long-term follow-up; MSM = males who have sex with males; RCT = randomized, controlled trial.

1. Giuliano AR et al. *N Engl J Med.* 2011;364:401–411. 2. Palefsky JM et al. *N Engl J Med.* 2011;365:1576–1585. 3. Goldstone S et al. EUROGIN 2018. FC 4-2.

Immunogenicity of 4vHPV Vaccine in Adult Males 27–45 Years of Age¹



Evidence

Previously treated for HPV:
now 10 papers



Efficacy of the 4vHPV Vaccine to Prevent **CIN2/3** Recurrence in Adult Females With Previous Disease

Females aged 20–45 years
vaccinated after
LEEP for CIN2/3
Kang et al 2013¹

71%

reduced rate of
recurrent CIN2/3^a

Kang WD et al. *Gynecol Oncol.* 2013;130:264–268

Females aged 18–45 years
vaccinated after
LEEP for CIN2+
Ghelardi et al 2018²

81%

reduced rate of
recurrent CIN2+

Ghelardi A et al. *Gynecol Oncol.* 2018;151:229–234

Females aged 45 years with a
history of HPV disease^b
Pieralli et al 2018³

75%

reduced rate of
recurrent disease

Pieralli A et al. *Arch Gynecol Obstet.* 2018;298:1205–1210

^aRelated to HPV types 6, 11, 16, and 18.

^bWomen previously treated for cervical squamous intraepithelial lesion.

4vHPV = 4-valent human papillomavirus; CIN = cervical intraepithelial neoplasia; LEEP = loop electrosurgical excision procedure.

1. Kang WD et al. *Gynecol Oncol.* 2013;130:264–268. 2. Ghelardi A et al. *Gynecol Oncol.* 2018;151:229–234. 3. Pieralli A et al. *Arch Gynecol Obstet.* 2018;298:1205–1210.

Efficacy of the 4vHPV Vaccine to Prevent **EGW** Recurrence in Adult Females With Previous Disease¹



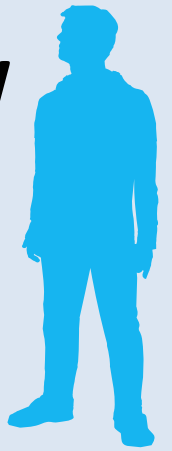
Females 20–45 years
vaccinated after LEEP for CIN2/3
Ghelardi et al 2018¹

71%

reduced rate of
recurrent EGW

Ghelardi A et al. *Gynecol
Oncol.* 2018;151:229–234

Efficacy of the 4vHPV Vaccine to Reduce **HG-AIN** and **EGW** Recurrence in Adult Males With Previous Disease



Males (MSM) aged ≥ 20 years
with previous HGAIN
Swedish et al 2012¹

52%
reduced risk of
recurrent HGAIN

Swedish KA et al. *Clin Infect Dis.* 2012;54:891–898

Males (MSM) with previous
anal condyloma
Swedish et al 2014¹

50%
reduced risk of
recurrent anal condyloma

Swedish KA et al. *PLoS One.* 2014;9:e93393

Publicly Funded HPV Immunization Programs in Canada: Recent additions

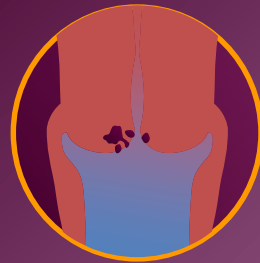
Province	Program
Manitoba¹	<p>School program: Males/Females Grade 6 (2 dose); Catch up program: F: Born 1997 or later; M: Born 2002 or later; High-risk program: HIV+ and immunocompromised M:9-26 /F:9-45; Dx RRP (past or present); Men < 18 incarcerated (past or present), Gay bisexual male & Transgender 9-26; Sexual assault victims M:9-26/F:9-45; Females 9-45 with new high-grade cervical histopathology</p>
Prince Edward Island²	<p>School program: Males/Females Grade 6 (2 dose); Catch up program: Individuals who missed the HPV immunization in Grade 6 since 2007; High-risk program:</p> <p>Adult males: 18-26 with following risk factors</p> <ul style="list-style-type: none"> • having unprotected sex with multiple partners (male and female) • history of genital warts • individuals who missed the HPV immunization in Grade 6 since 2012 <p>Men who have sex with men (MSM) and for immunocompetent males and females who have HIV regardless of age</p> <p>Adult females: 18 to 45 with the following risk factors</p> <ul style="list-style-type: none"> • having unprotected sex with multiple partners (male and female) • history of genital warts • an abnormal PAP test
Alberta³	<p>School program: Males/Females Grade 6 (2 dose); Catch up program: Students eligible to receive vaccine in Grade 6 continue to be eligible to receive the vaccine up to and including 26 years of age; Males and females 17 years up to and including 26 years of age.</p> <p>High-risk program: Hematopoietic Stem Cell Transplant recipient: less inclusive as catch-up program; Organ transplant candidates and recipients: less inclusive as catch-up program</p>

Counselling Adults for HPV Vaccination

Counseling for Adult HPV Vaccination



This is a vaccine
to protect you
against ***cancer***



HPV cancers are
preventable



We don't want
your family to
***lose you to this
disease***

Counselling for Adult HPV Vaccination:

- ❖ Don't assume a young adult was vaccinated in school or clinic-based program
- Remember adults are or will become parents
- When you counsel adults for HPV vaccination, they are more likely to consent for their children

Provincial HPV Vaccination Programs During COVID-19

- Second dose of HPV vaccine was not given as schools were shut down (March 2020)
- Most logical option is 2nd dose will be delivered in fall (at 12 months) when next cohort gets their 1st dose

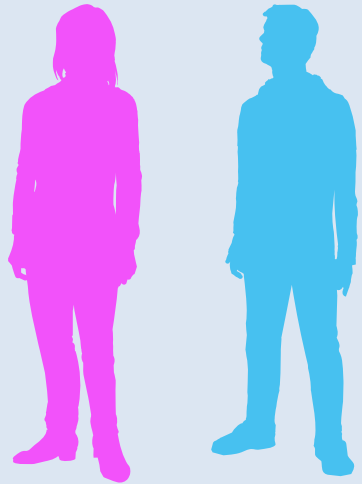
HPV Vaccination During COVID-19

- Many pharmacists and some GP offices are not doing vaccinations during COVID
- Missed or late doses – resume asap
- Can be given at colpo visit

HPV Vaccination Counselling – “the message”

keep it simple:

1. effective
2. safe
3. recommended



**It's never too late
to vaccinate!**



HPV infection is common in adults



Long-term vaccination efficacy in adults



**Immune compromised are at highest risk for HPV
and should be vaccinated**

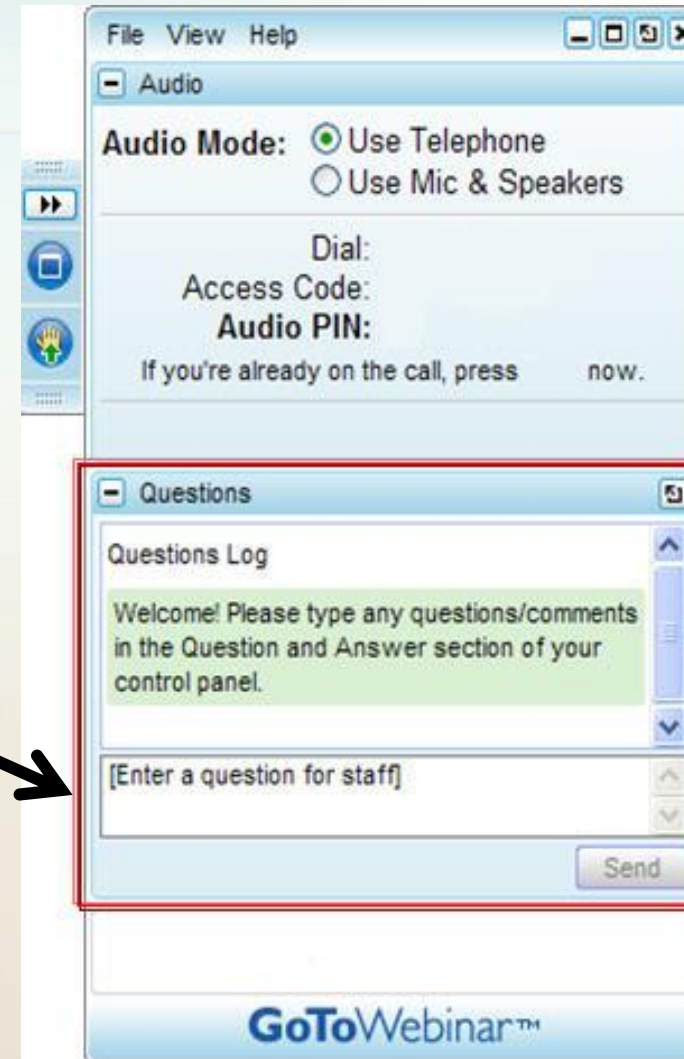


Vaccination efficacy in previously exposed adults

Question & Answer Period



Submit your text question using
the Questions pane



HPV Prevention in the Adult Population protecting those at higher risk



- **Evaluation:** <https://www.surveymonkey.com/r/XYG3PML>
- **Slide Set, Video recording, HPV documents at:** www.CIDCgroup.org
- Find out about news and upcoming events....

....Join the **Canadian HPV Prevention Network** at: www.CIDCgroup.org

Thank you for participating!

More Info: George Wurtak, Executive Director, GWurtak@CIDCgroup.org

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