Consortium for Infectious Disease Control

A neutral, third party platform supporting infectious disease projects, providing continuing medical education, coordinating initiatives, and undertaking research

Winnipeg, Manitoba, Canada
November 25, 2020

www.CIDCgroup.org

If women are from Venus and men are from Mars, are HPV infections also different?

Dr. Angel Chu, MD, FRCPC

Clinical Assistant Professor, Cumming School of Medicine

Medical Director, Calgary STI Clinic

Moderator: Dr. Marc Steben MD, DESS, CCFM, FCFM

Chair of the Canadian Network on HPV Prevention
Family Physician, Family Medicine Group La Cité du Parc Lafontaine, Montreal, QC
Member, Canadian STI Guidelines Expert Group
Board Member, International Papillomavirus Society

Organizer: George Wurtak BSc, MED

Executive Director, Consortium for Infectious Disease Control Winnipeg, MB
Director, Canadian Network on HPV Prevention
Founding Chair, International Indigenous HPV Alliance

This educational program is made possible through the support of **Merck Canada Inc.**
and with assistance by BD Diagnostics and Immunize Canada

Webinar Objectives

- Review the differences between males and females in terms of burden of disease and epidemiology of HPV infections
- Discuss the latest clinical data and recommendations for HPV immunization in males and females
- Discuss the challenges and opportunities providers face when immunizing males versus females

Administrative Information

How to participate:

- You can hear the audio for today's webinar via your computer by selecting "Use Mic & Speakers"
- Or, to join by phone, select "Use Telephone" in your Audio window. Info for dial in then will be displayed
- Submit your text question using the Questions pane & click 'Send' button
- Questions will be answered at the end of the presentation

- Submit at any time by typing in the "Questions" pane on the control panel
- Questions will be answered following the presentation

Note: A recording of the presentation will be made available at www.CIDCgroup.org

Slides and Video Recording

The webinar **Slides and Recording** will be archived at:
https://www.CIDCgroup.org

Evaluation Survey:
https://www.surveymonkey.com/r/PH8C3RW

Completion of survey is requested – all registered participants will receive an email with this link

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

Dr. Angel Chu, MD, FRCPC

- **Clinical Assistant Professor, Cumming School of Medicine**
- **Medical Director, Calgary STI Clinic**

If women are from Venus and men are from Mars, are HPV infections also different?

Dr. Angel Chu
MD, FRCPC
Clinical Assistant Professor, Cumming School of Medicine
Medical Director, Calgary STI Clinic

Presenter Disclosures

- Presenter: Dr. Angel Chu, MD, FRCPC, Clinical Assistant Professor, University of Calgary

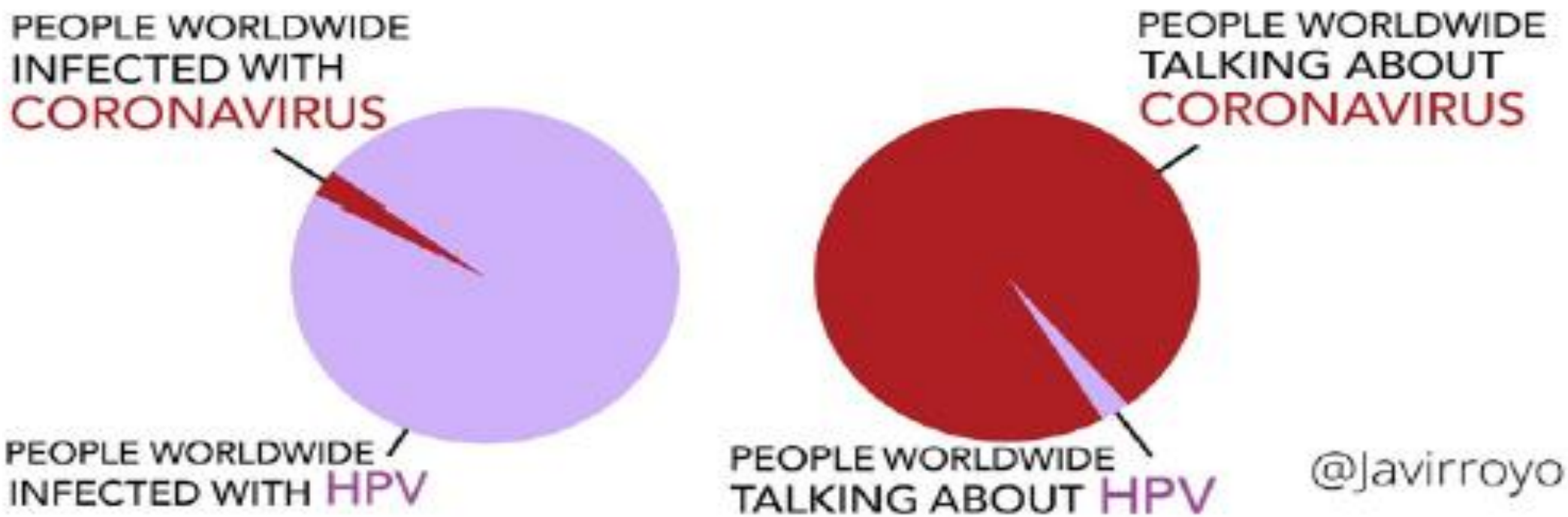
- Relationships with commercial interests:
  - **Grants/Research Support:** Calgary Lab Services
  - **Speakers Bureau/Honoraria:** Merck, Pfizer, Sanofi Pasteur, AVIR, FMWC, Immunize Canada
  - **Consulting Fees:** Merck, Pfizer, GSK, Sanofi Pasteur

Objectives

- Review the differences between males and females in terms of burden of disease and epidemiology of HPV infections
- Discuss the latest clinical data and recommendations for HPV immunization in males and females
- Discuss the challenges and opportunities providers face when immunizing males versus females

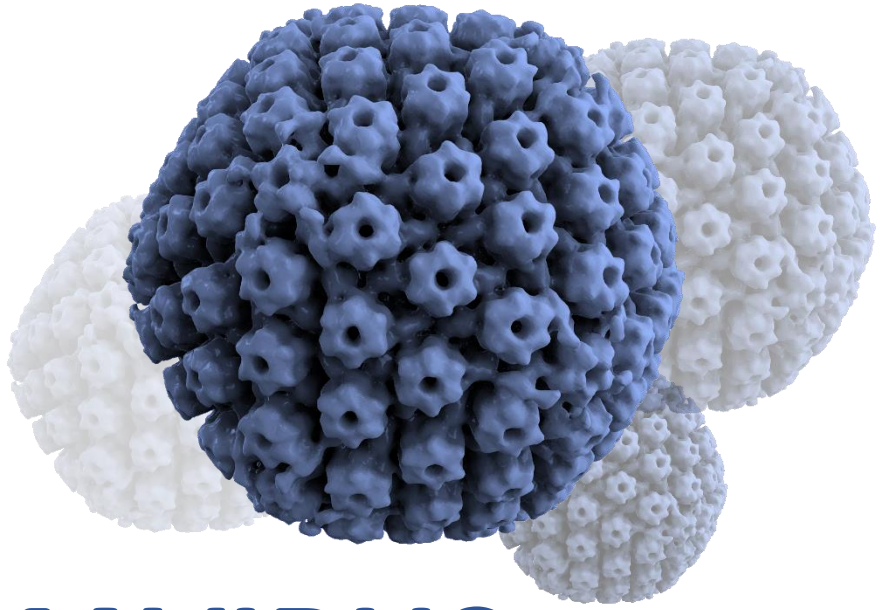
COVID-19 Won't Be the Last (Or Worst) Pandemic: It's Time to Build Resilience Into Our Cervical Cancer Elimination Goals

Marc Steben, MD;[1] Teresa Norris;[2] Zeev Rosberger, PhD[3], on behalf of HPV Global Action *



WHAT IS HPV

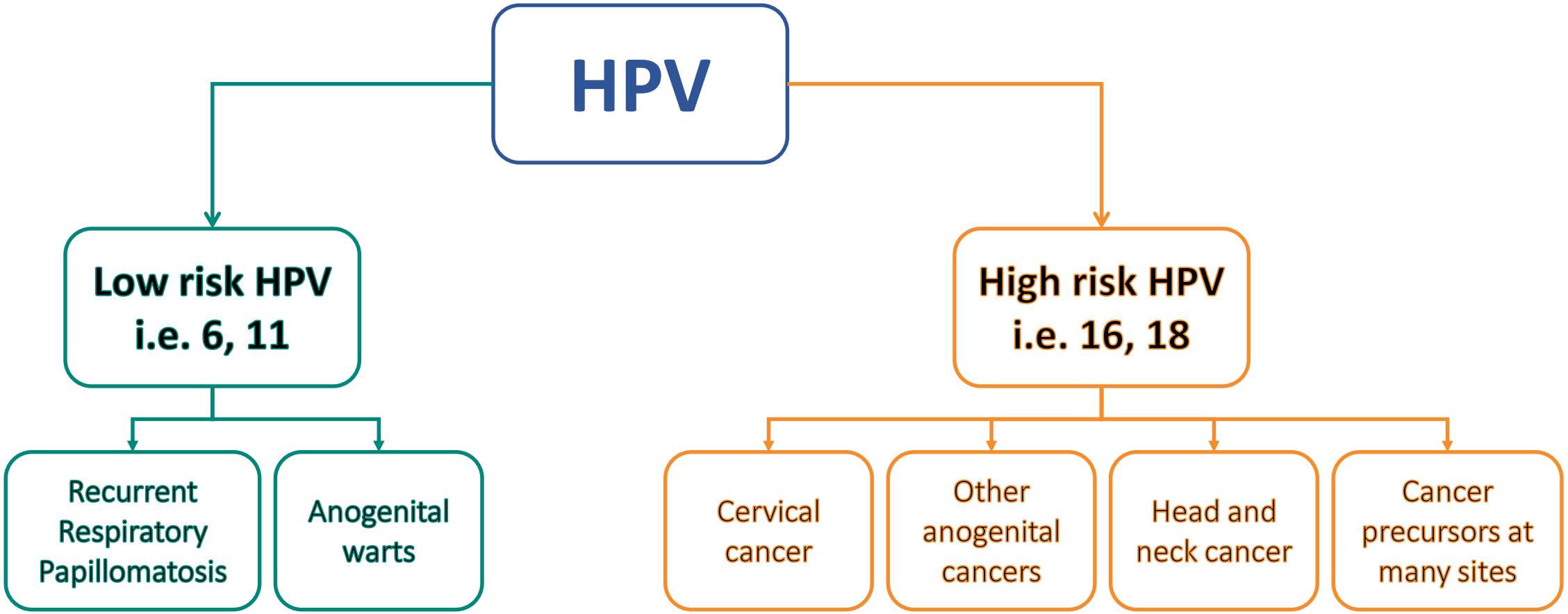
HUMAN PAPILLOMAVIRUS



HPV IS SEXUALLY TRANSMITTED CANCER

also known as the Human Papilloma virus, **affects both men and women.** **Over 80 types of HPV** have been identified. Some strands have been found to cause **cervical cancer, oral cancer, penile cancer and anal cancer.** There a definitive link between **oral sex** and **oral cancer.** Studies show that **men are 35% more likely** to develop HPV-related oral cancer than women. Between 1973 and 2004, the the incidence of HPV-related oral cancers among people in their 40s **nearly doubled.** Doctors estimate that HPV the primary cause of the estimated **5,600 cancers** that are found each year in the **tonsils, lower tongue and upper throat.** The American Cancer Society estimates that in 2006, over **9,700 women were diagnosed with cervical cancer**, and 3,700 women died from it in the United States. Of an estimated 28,900 cases of oral cancer a year, **18,550 are in men.** Studies have shown that among active teens, 80% of oral sex is unprotected. The prevalence of high-risk genital HPV in women in the U.S. **is highest in the 14- to 19-year-old** age groups. About 20 million people in the U.S. are currently infected with HPV. Studies show that **the Human Papilloma virus** is through **direct contact** Each year another 6.2 get a new HPV infection. An estimated **one million** sexually active people in the United States currently have visible genital warts It is estimated that **80 percent of all women** and 50% of men and women combined will get **at least one type** of genital HPV. The **No. 1 risk factor** for getting HPV is a high number of sexual partners.

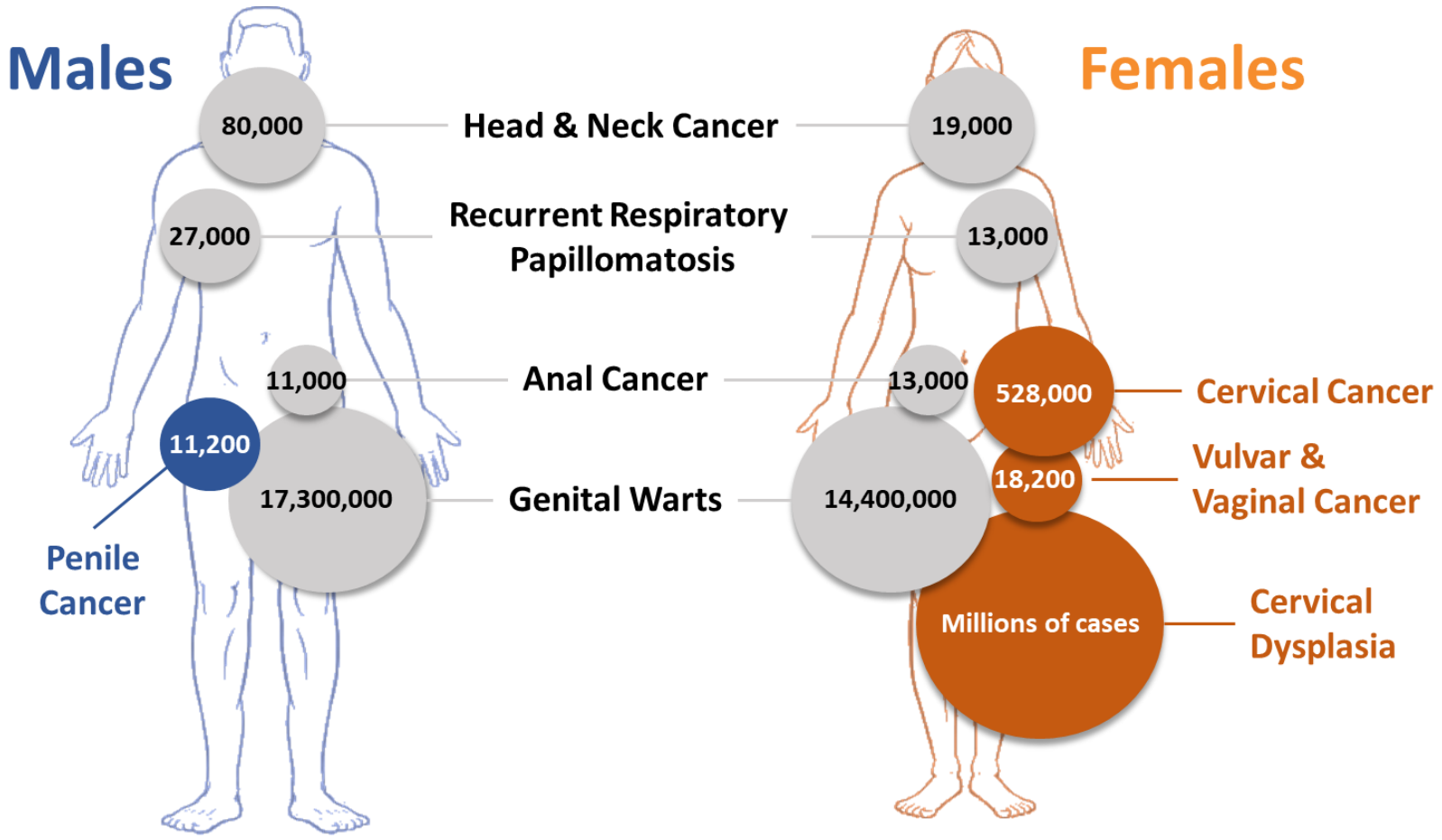
Diseases Caused by HPV



IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 90
https://publications.iarc.fr/Book-And-Report-Series/Iarc-Monographs-On-The-Identification-Of-Carcinogenic-Hazards-To-Humans/Human-Papillomaviruses-2007

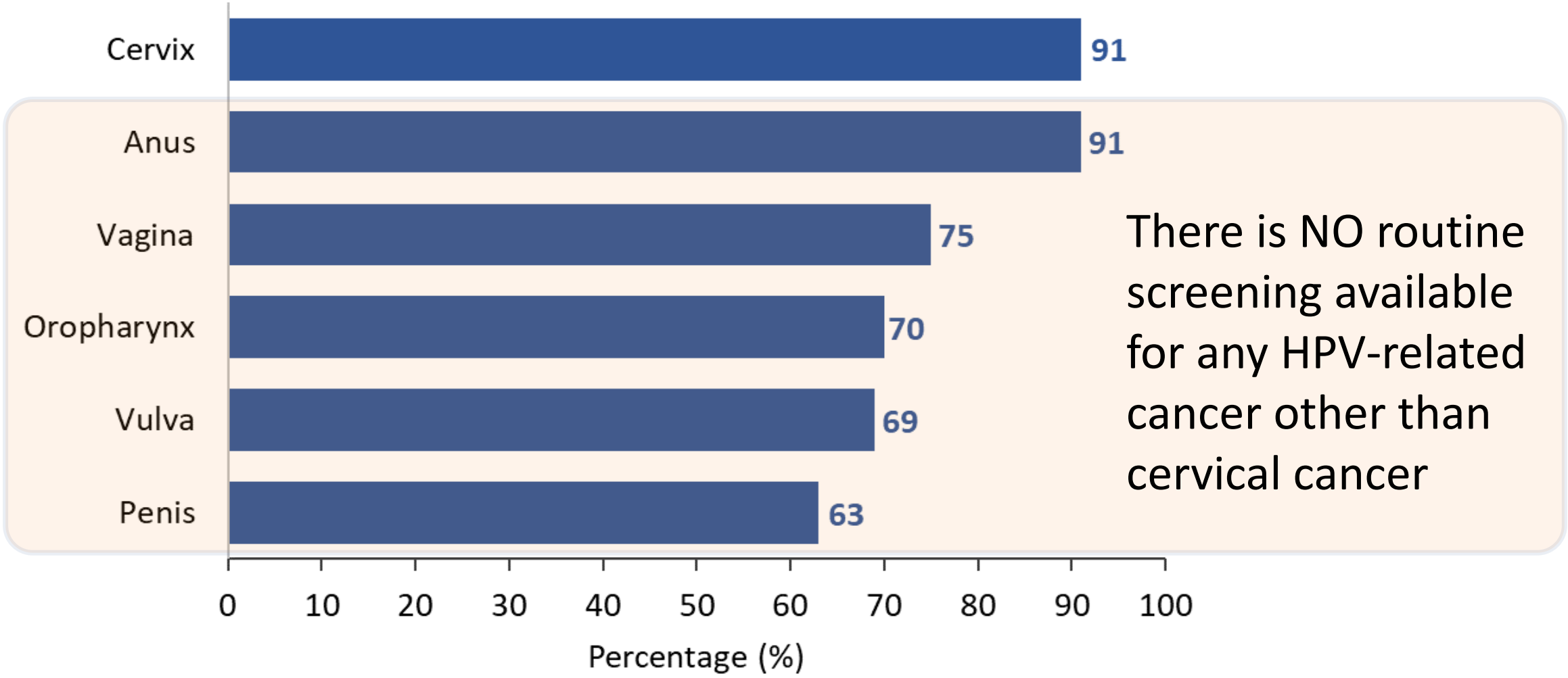
Burden of HPV-Associated Diseases

Worldwide HPV is estimated to cause 1/20 cancers in men and women[1–13]



Please refer to slide notes for references

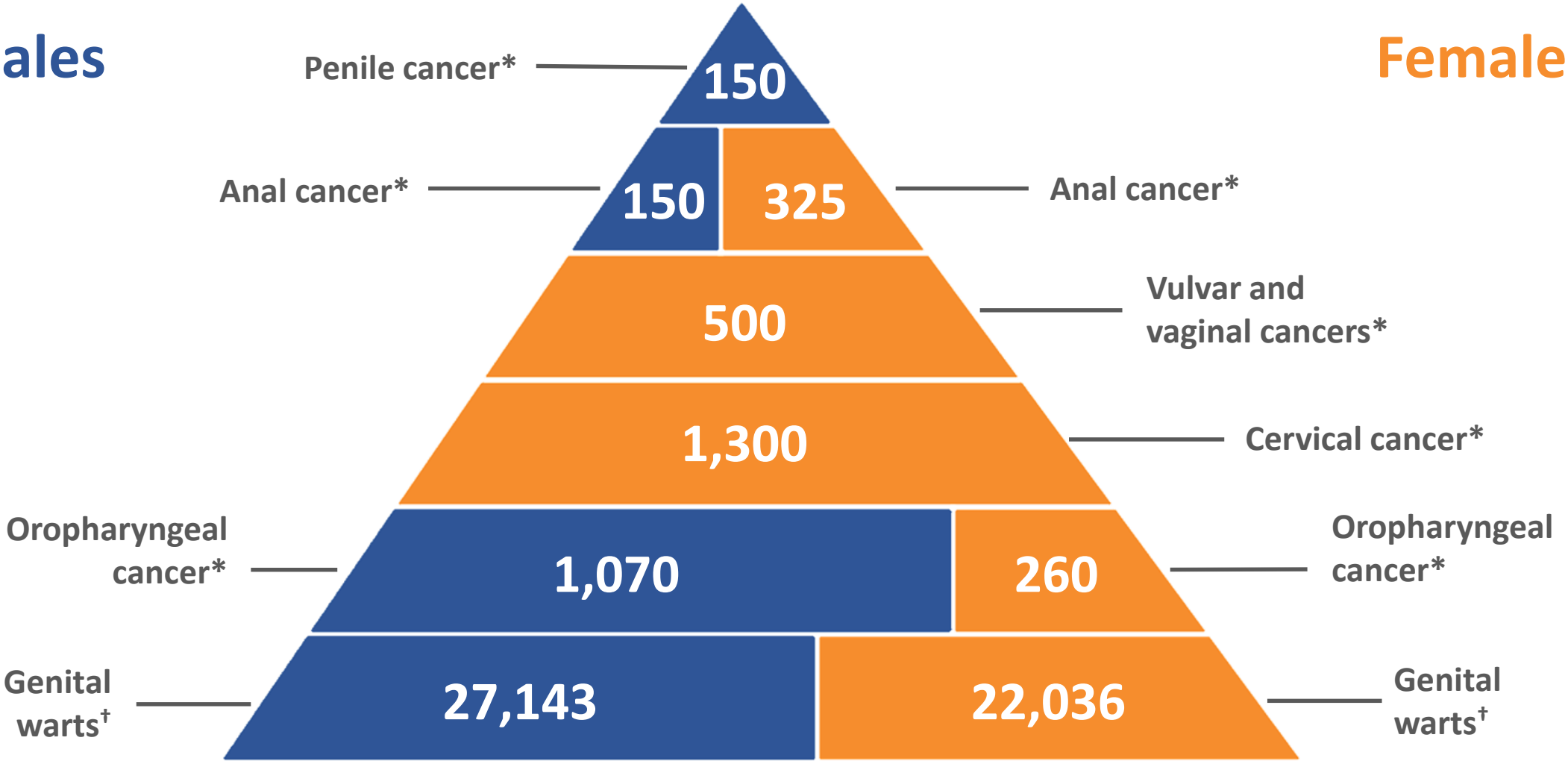
Estimated HPV Contribution in Cancer



There is NO routine screening available for any HPV-related cancer other than cervical cancer

https://www.cdc.gov/cancer/hpv/statistics/cases.htm reviewed by September 3, 2020

Canadian Burden of HPV-Associated Diseases

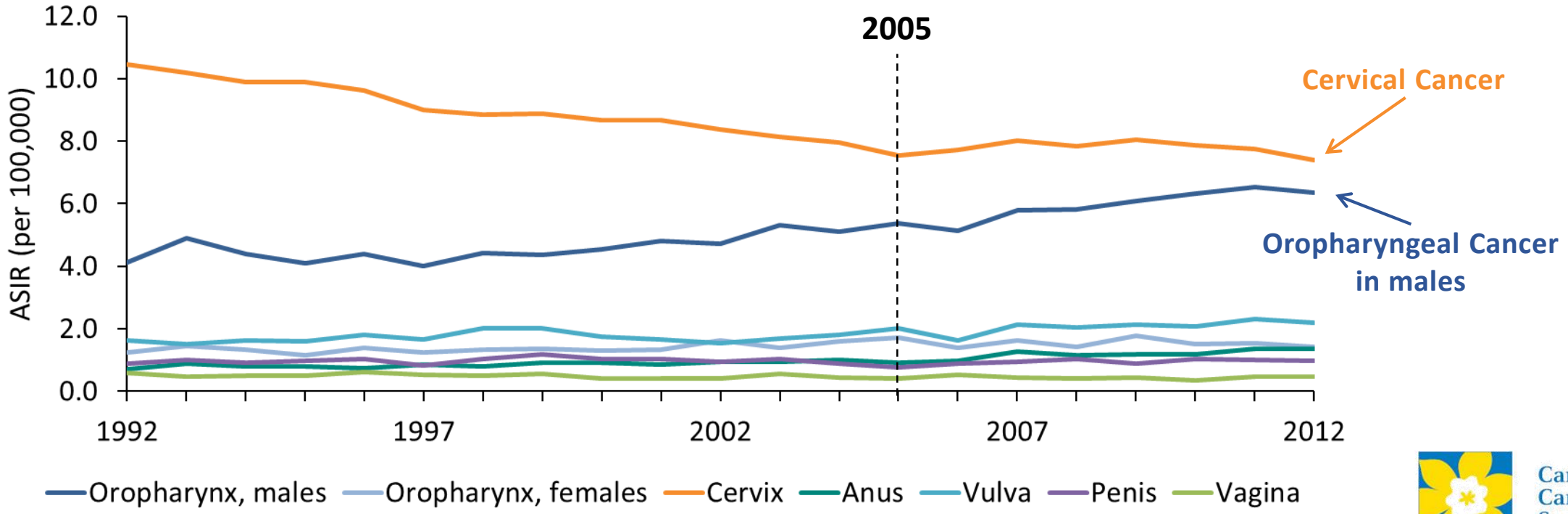


* Based on Canadian incidence rates in 2012; † Based on an incidence in Manitoba in 2004 and generalized to Canada of 1.54/1,000 males and 1.23/1,000 females and 2015 Canadian census data.
Canadian Cancer Statistics 2016. Special topic: HPV-associated cancers. Canadian Cancer Society, Government of Canada. October 2016.

Incidence of HPV-Associated Cancers in Canada

- The rate of **cervical cancers** decreased between 1992 and 2005, and remained relatively stable thereafter.
- The rate of **oropharyngeal cancers** has increased significantly: **3.1% increase** in males per year
  1.1% increase in females per year
- In 2012: **oropharyngeal cancer cases: 1335**; **cervical cancer cases: 1300**

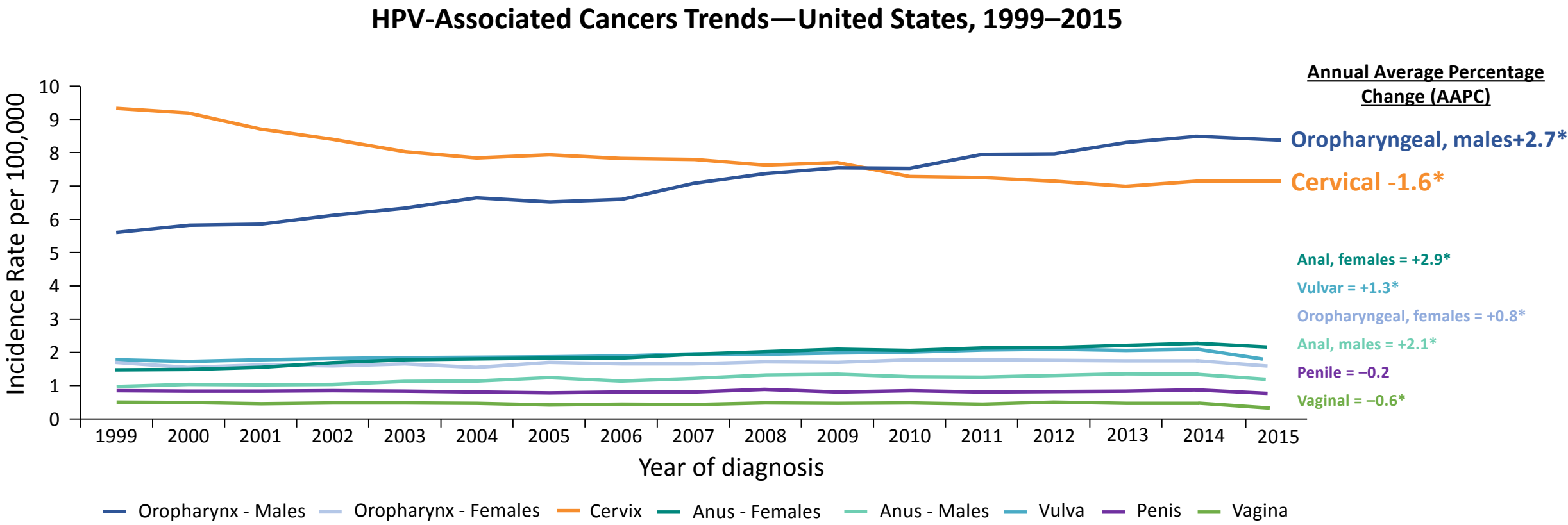
Trends in age-standardized incidence rates (ASIR) for HPV-associated cancers Canada,1992-2012§



§ Quebec data are available to 2010; Canadian Cancer Statistics 2016

Canadian Cancer Society

HPV-Related Oropharyngeal Cancers in Males Exceeds Cervical Cancers in Females in the US

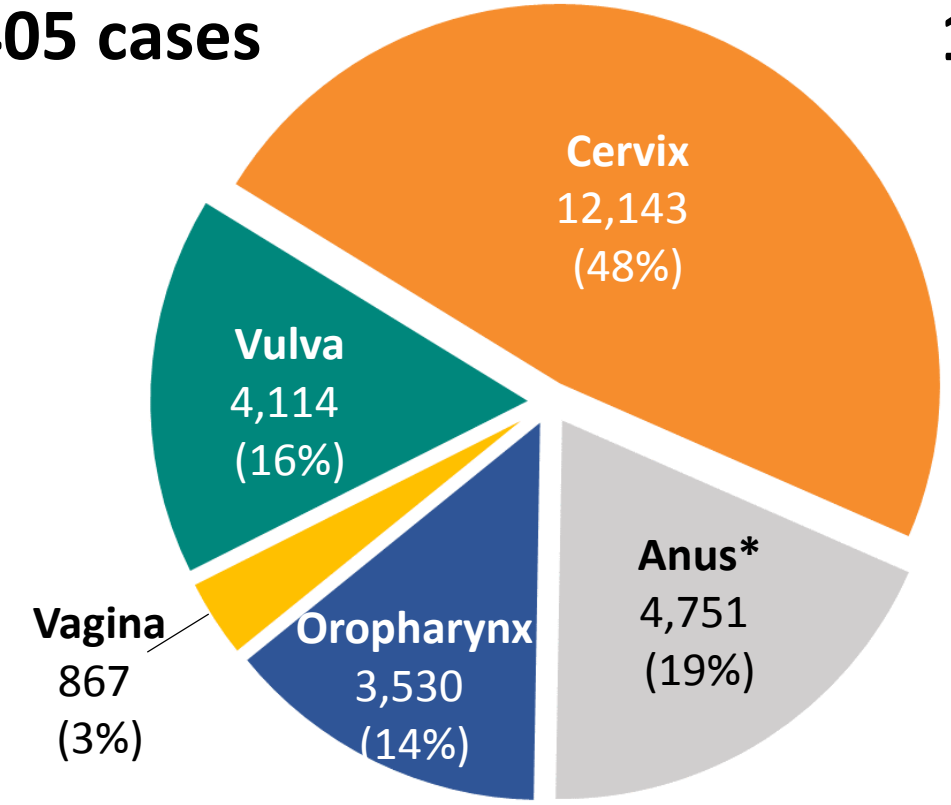


Rates were considered to increase if AAPC >0 (P<0.05) and to decrease if AAPC <0 (P<0.05); otherwise rates were considered stable. *P<0.05.

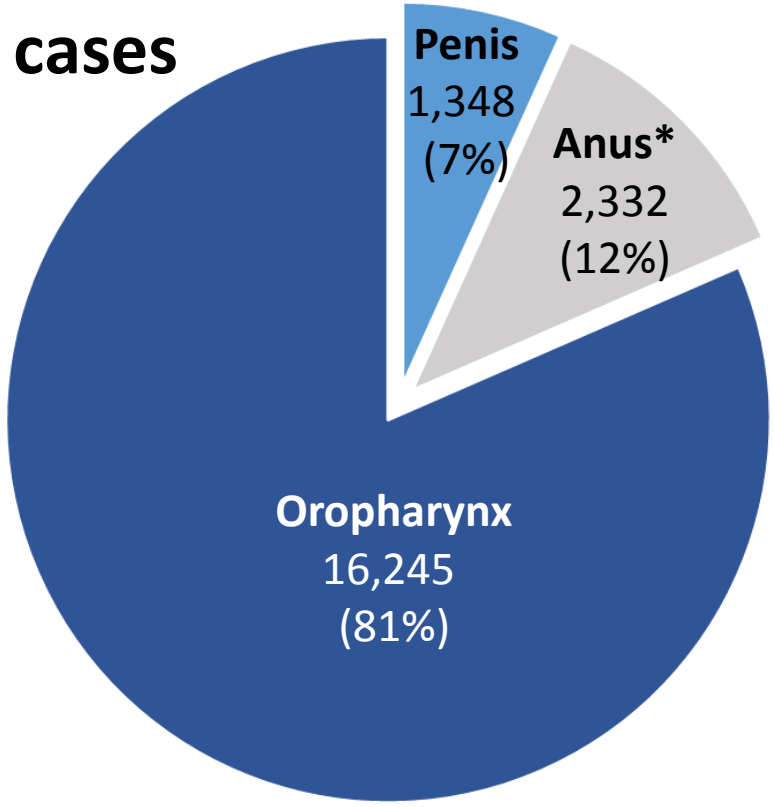
Van Dyne E, Henley SJ, Saraiya M, et al. Trends in human papillomavirus-associated cancers—United States, 1999–2015. *MMWR Morbid Mortal Wkly Rep*. 2018;67(33):918–924. https://www.ncbi.nlm.nih.gov/pubmed/30138307

Annual Number of New HPV-Associated Cancer Cases in the US, 2013-2017

Females
25,405 cases

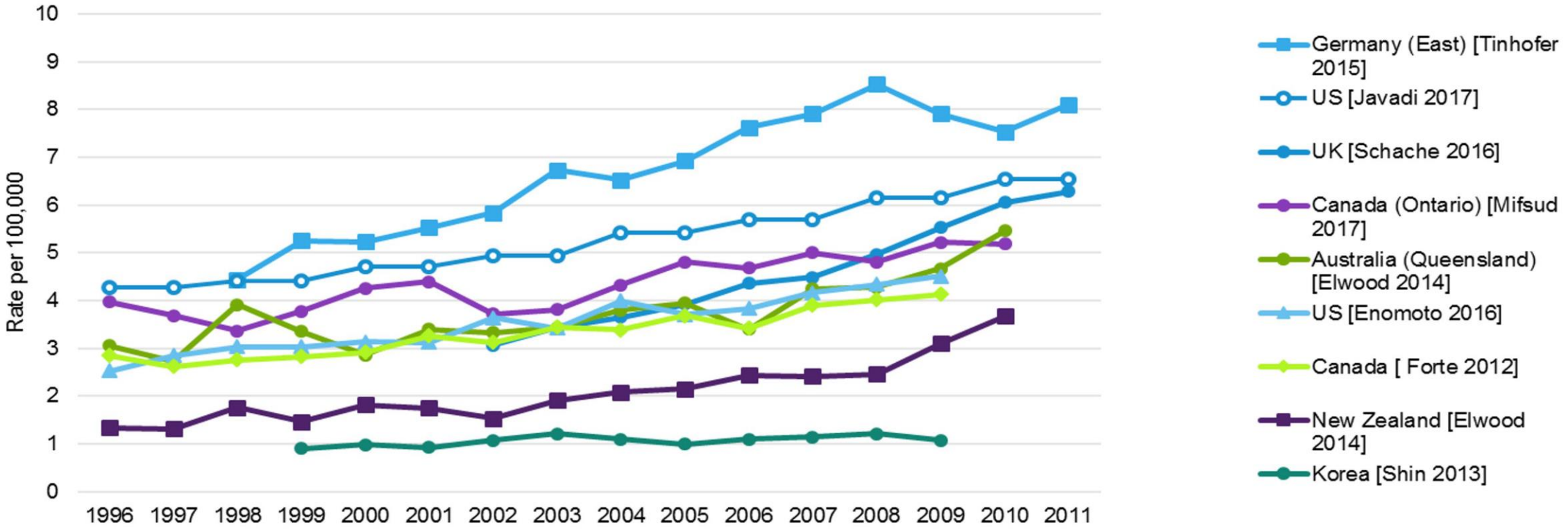


Males
19,925 cases



*Includes anal and rectal squamous cell carcinomas.
www.cdc.gov/cancer/hpv

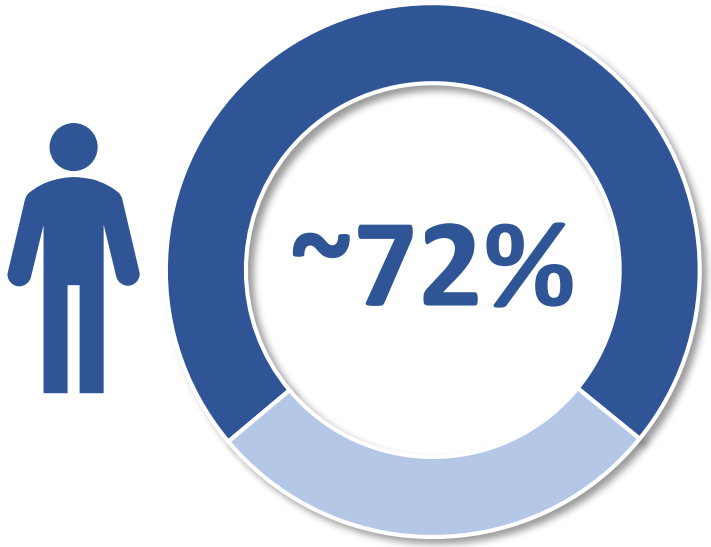
Global Incidence Trend of Oropharyngeal Cancer in Males

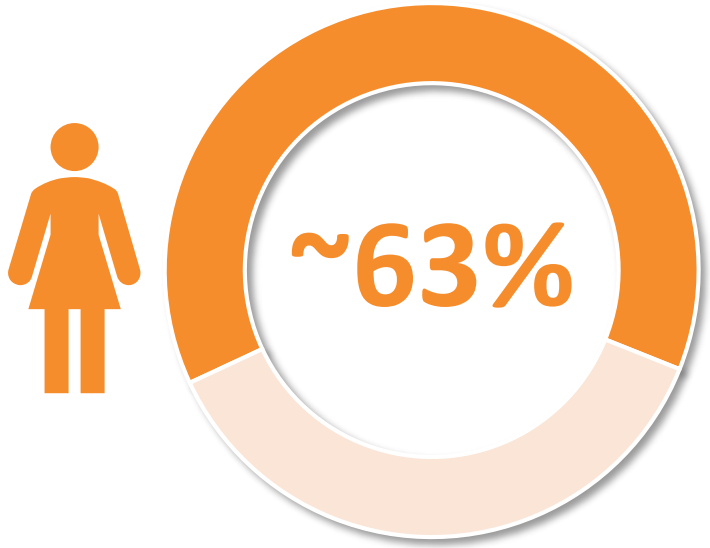


Morais et al. Presented at ICHNO; March 2019; Barcelona

HPV Attribution in Head & Neck Cancers: US

The Centers for Disease Control and Prevention (CDC) estimates that approx. **70%** of oropharyngeal cancer cases overall are probably caused by HPV

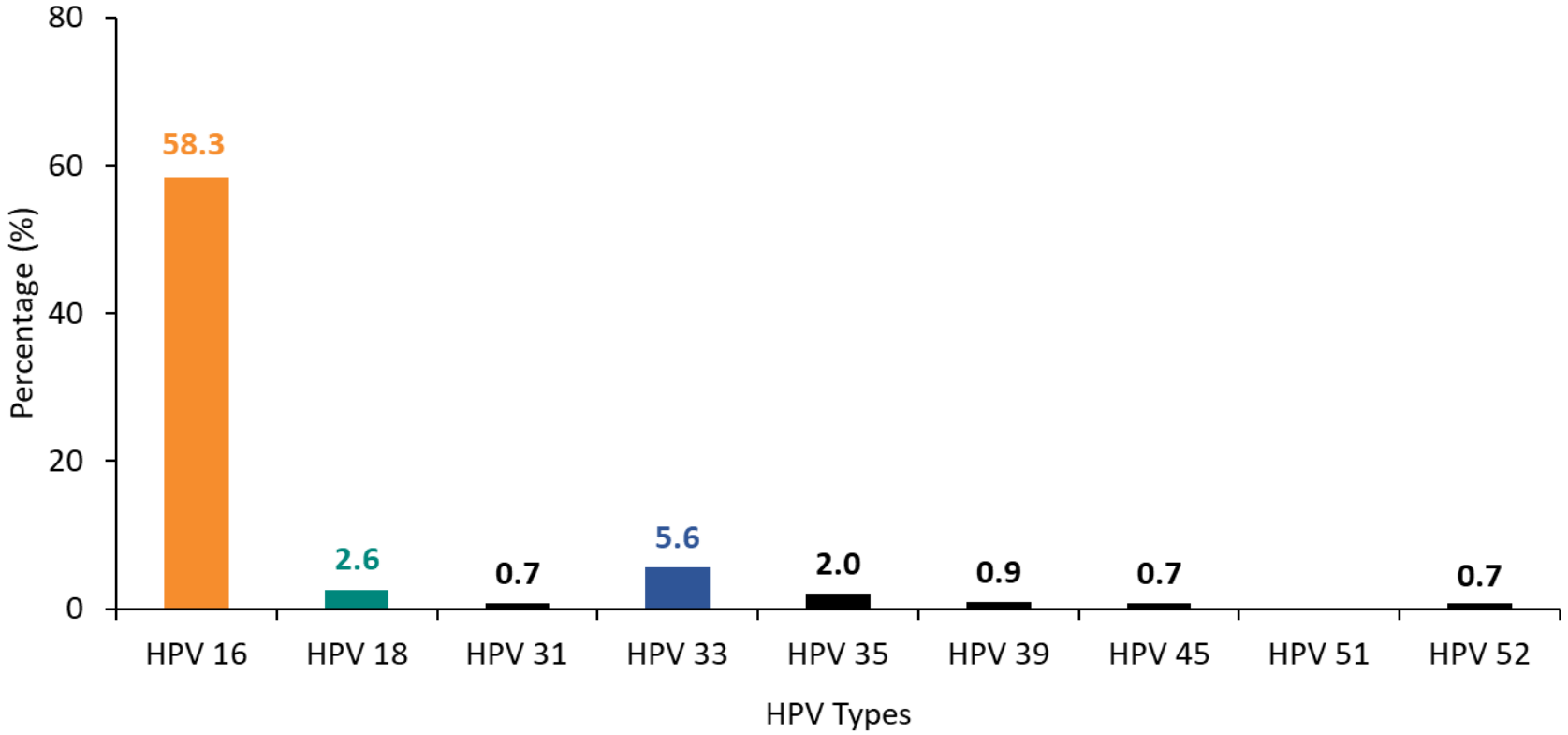




CDC. 2018 HPV & Cancer. How Many Cancers are Linked to HPV Each Year?. https://www.cdc.gov/cancer/hpv/statistics/cases.htm

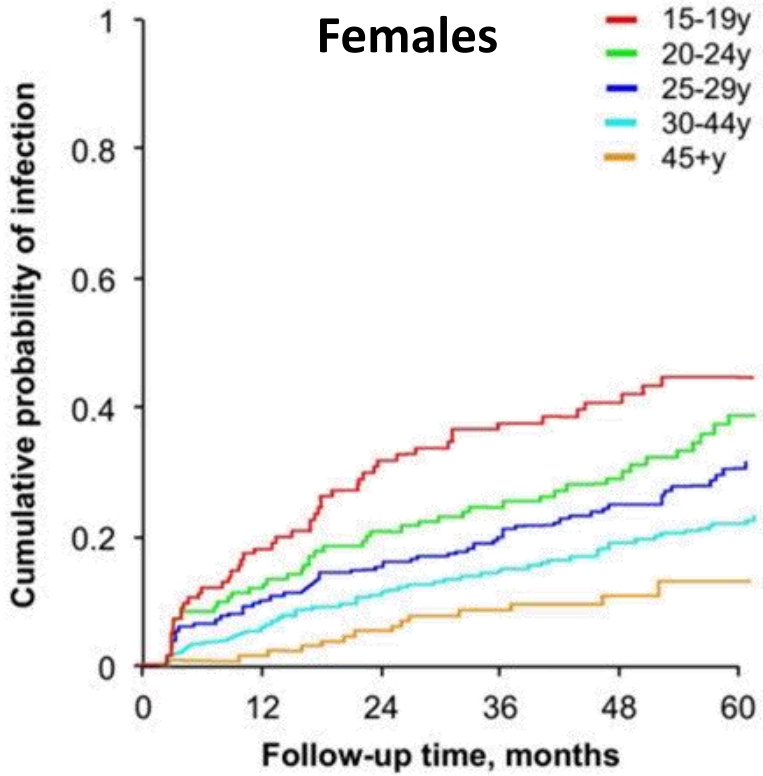
HPV-16 is the Most Common Type Found in Oropharyngeal Cancers: US

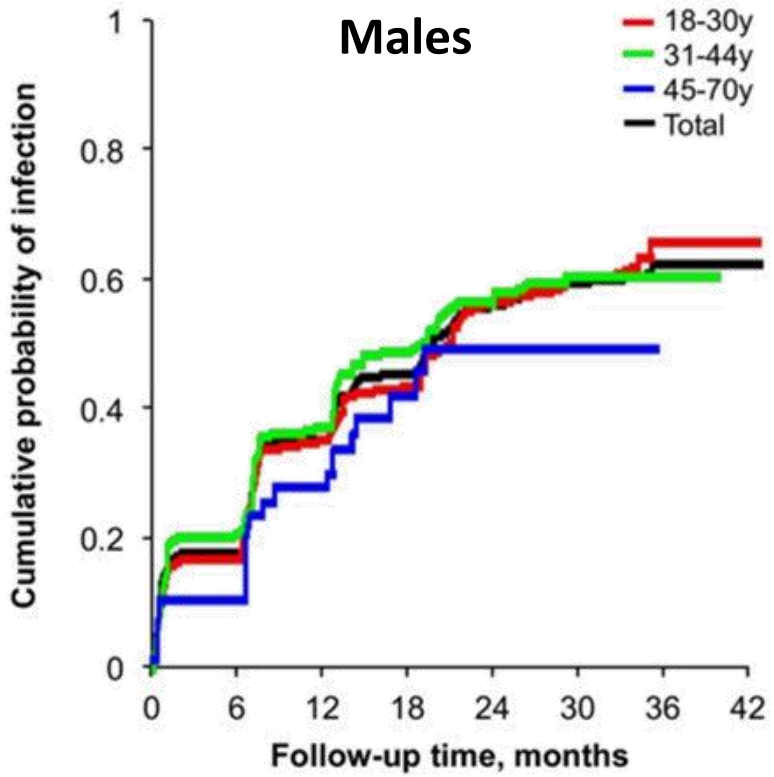
Attribution of Most Common Oncogenic HPV Genotypes Detected in Oropharyngeal Cancer



Saraiya M, Unger ER, Thompson TD, et al. US assessment of HPV types in cancers: implications for current and 9-valent HPV vaccines. *J Natl Cancer Inst*. 2015;107(6):djv086.

Genital HPV Infections by Age

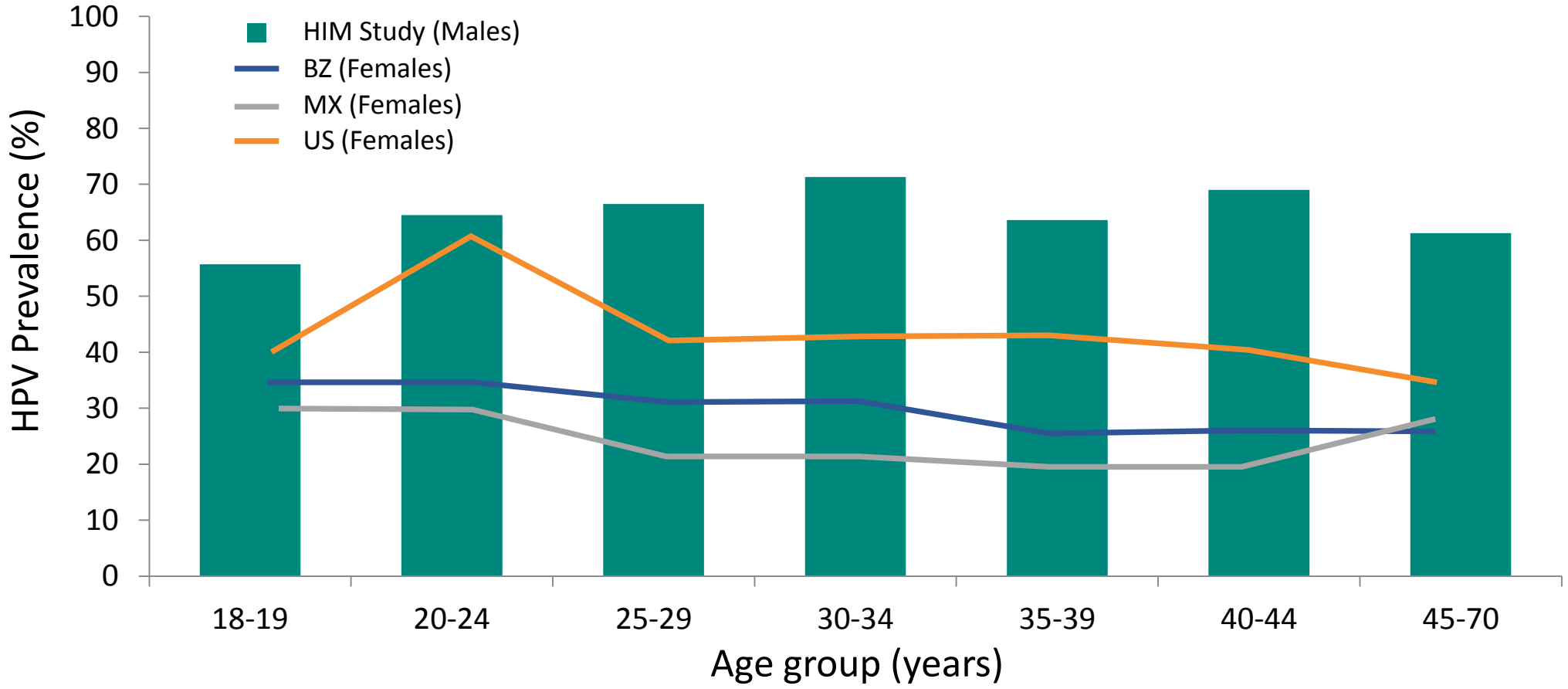




The rate of acquiring a new genital HPV infection decreases with age in females but does not vary by age in males

Giuliano AR et al. Int J Cancer. 2015 Jun 15;136(12):2752-60.

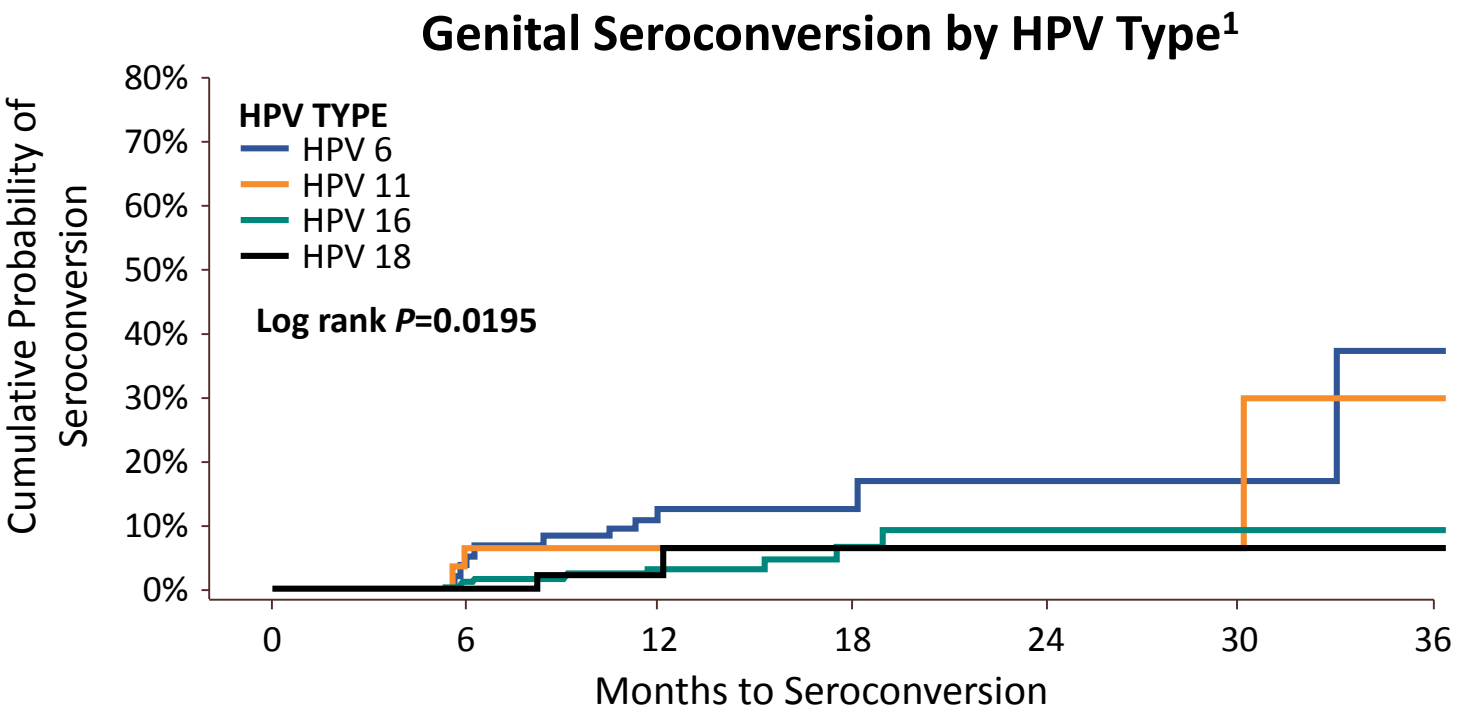
Genital HPV Prevalence is Higher in Males than Females Across all Age Groups



BZ, Brazil; HIM, HPV Infection in Men; MX, Mexico; US, United States

1. Giuliano AR et al. *Cancer Epidemiol Biomarkers Prev*. 2008;17:2036-43; 2. Dunne EF et al. *JAMA*. 2007;297:813-19; 3. ICO/IARC HPV Information Centre on HPV and Cancer. http://www.hpvcentre.net/datastatistics.php. Accessed June 4, 2018.

Males have a Low Rate of Seroconversion Following Genital HPV Infection



% Seroconversion		
Type	**Males[1]**	**Females[2]**
HPV6	19.3%	68.8%
HPV11	8.6%	NA
HPV16	3.6%	59.5%
HPV18	3.4%	54.1%

1. Giuliano AR et al. *Papillomavirus Res*. 2015;1:109-15.; 2. Carter et al. J Infect Dis. 2000 Jun;181(6):1911-9.

Natural HPV Antibodies Do Not Reduce The Risk of Subsequent Oral HPV Infection in Healthy Males

- Males with circulating serum antibodies to HPV 6, 11, 16, or 18, which are believed to provide partial protection against infection, **were not at lower risk** of acquiring oral HPV infection with the same HPV type

Association between baseline HPV serum antibody level and risk of incident type-specific oral HPV infection among HIM participants[a]

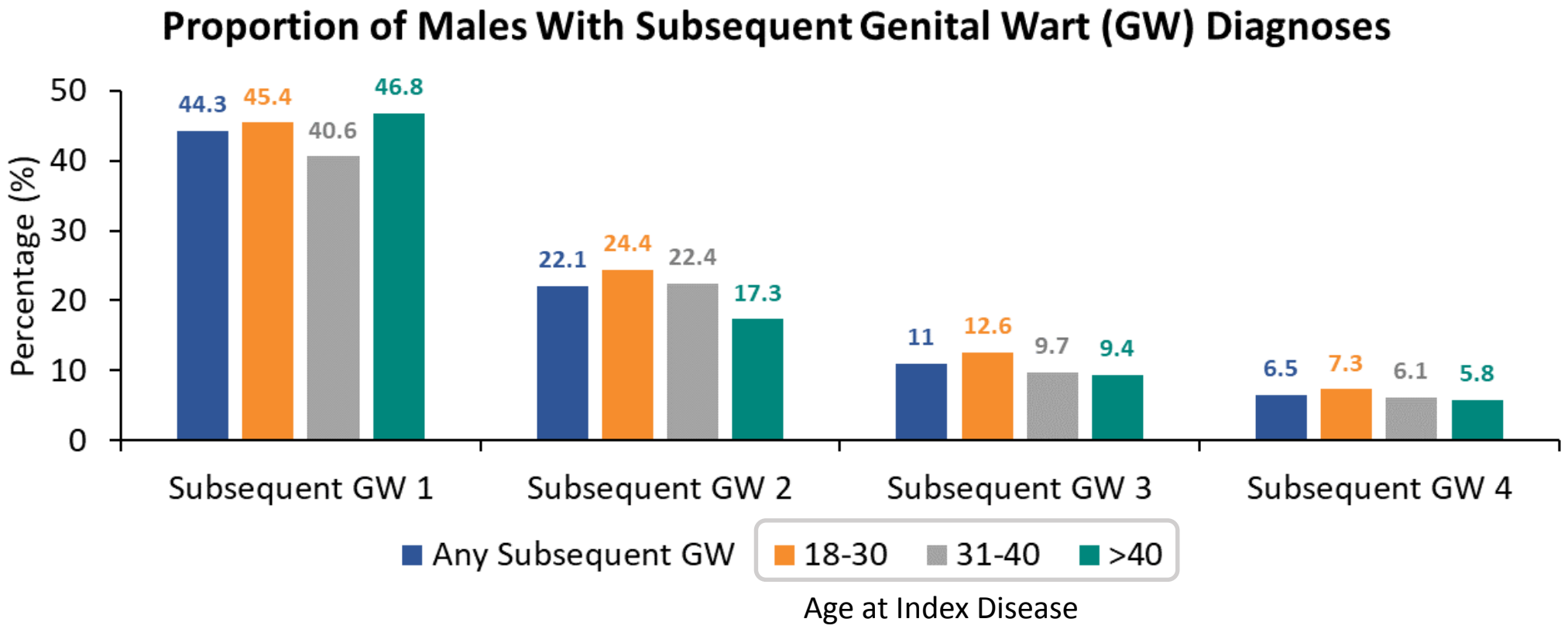
Serostatus at baseline	Any HPV type[b]			HPV 6		HPV 16	
	Infections, N	Univariate HR (95% CI)	Multivariable[b] aHR (95% CI)	Infections, N	Univariate HR (95% CI)	Infections, N	Univariate HR (95% CI)
Seronegative	21	1.00	1.00	6	1.00	14	1.00
Seropositive[c]	4	1.63 (0.56-4.76)	1.51 (0.49-4.69)	1	1.78 (0.21-14.78)	3	1.70 (0.49-5.90)

[a]Prospective study nested within HIM study evaluating whether natural HPV serum antibodies reduced the risk of oral HPV infection in 1,618 healthy males followed for a median of 12.7 months. [b]Adjusted for lifetime number of sexual partners (female and male). [c]Defined as positive >0.2, >0.3, >0.2, >0.2 OD units for HPV 6, 11, 16, or 18, respectively

aHR, adjusted HR; HIM, HPV Infection in Men; HR, hazard ratio

1. Pierce Campbell CM et al. *J Infect Dis*. 2016;214:45-48.

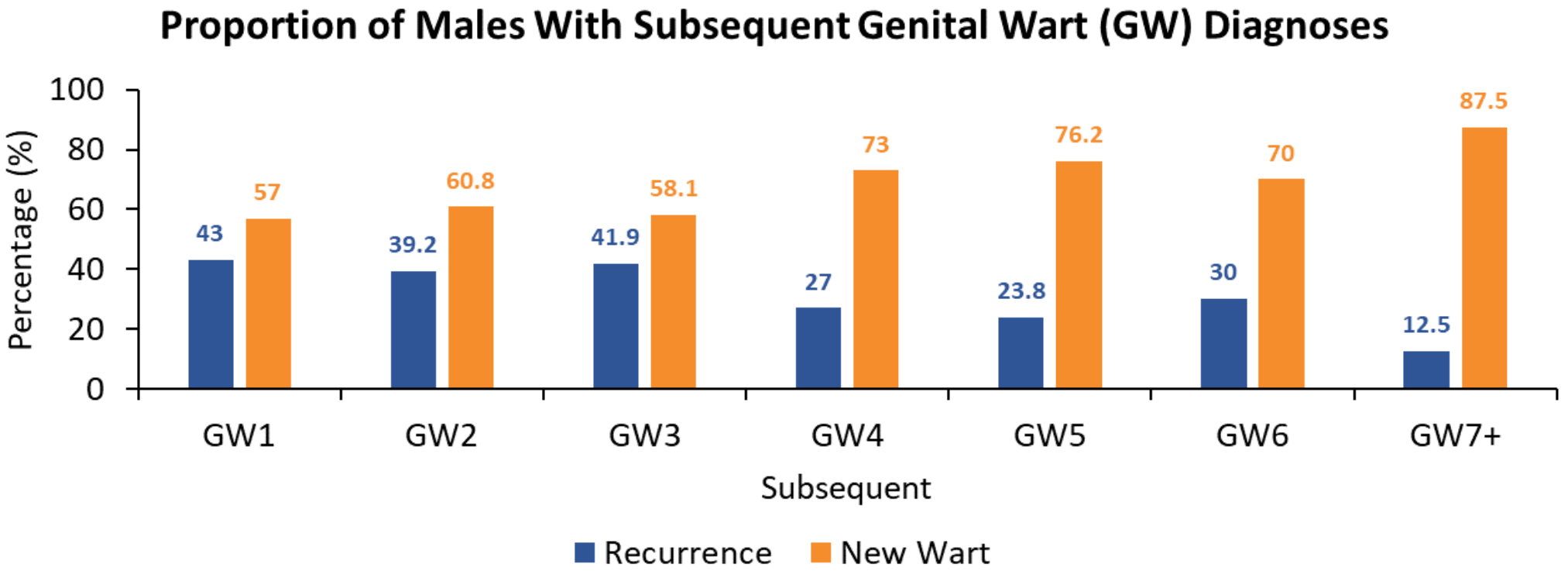
Genital Warts Recurrence in Males



- More than 44% of men experienced ≥1 genital warts following the initial episode
- The proportion of men with subsequent genital wart events did not differ by age at the index disease

Giuliano AR et al. J Infect Dis. 2019 Feb 15;219(5):703-710

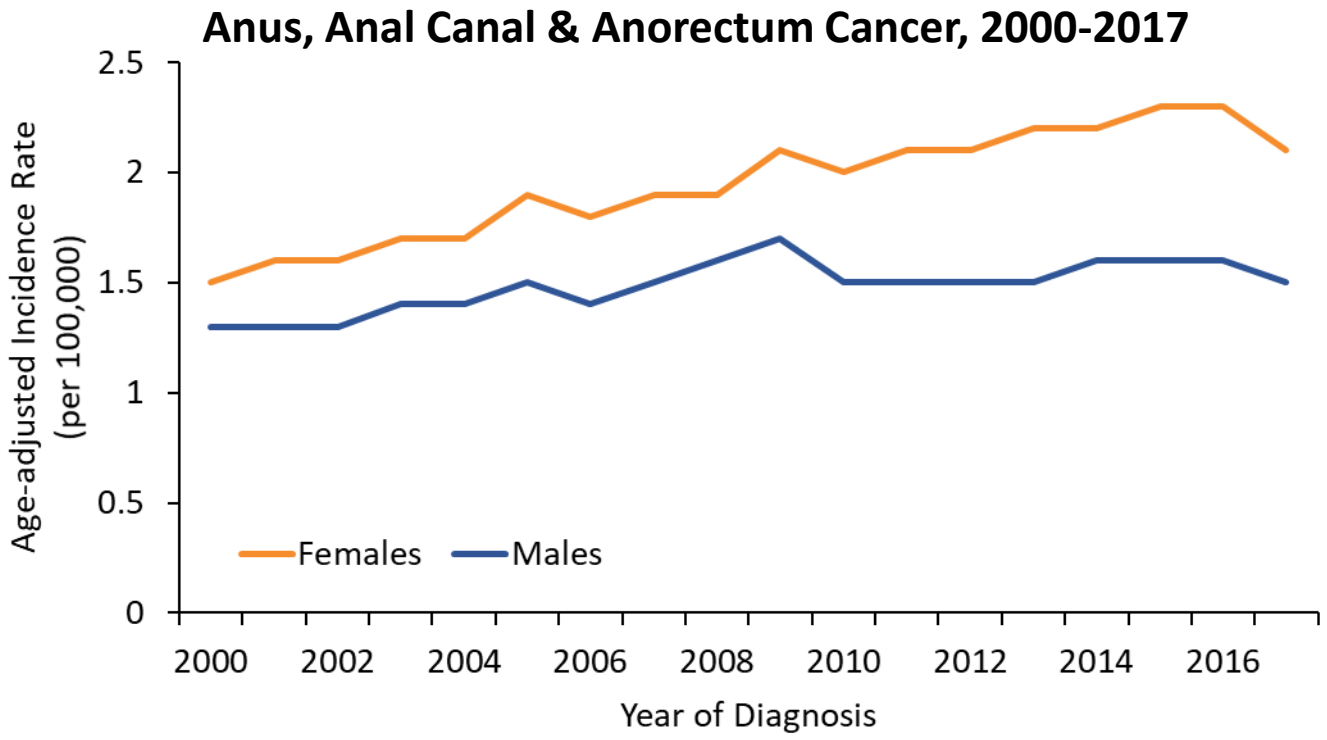
Genital Warts Recurrence in Males



The proportion of recurrent events significantly declined, and a concomitant rise in the proportion of new genital wart events was observed.

Giuliano AR et al. J Infect Dis. 2019 Feb 15;219(5):703-710

Increasing Anal Cancer Incidence in US Males and Females



Sex	Annual Percentage Change		
	Year Range	Estimate %	Direction
Females	2000-2015	2.7	↑
	2015-2017	-3.2	Stable
Males	2000-2017	1.2	↑

https://seer.cancer.gov/explorer/application.html?site=34&data_type=1&graph_type=2&compareBy=sex&chk_sex_3=3&chk_sex_2=2&race=1&age_range=1&stage=101&hdn_rate_type=1&advopt_precision=1&advopt_display=2

Incidence Rates of Cervical Cancer vs Anal Cancer in MSM

Disease		Incidence (per 100,000)
Cervical Cancer	before Pap screening[3]	**40-50**
	after Pap screening[3]	~8-10
Anal Cancer	in MSM, before onset of HIV epidemic[1,3]	**37**
	in HIV-positive MSM[1,2]	**~70-100**

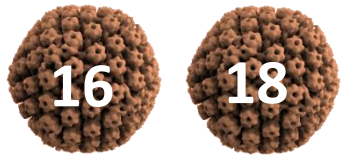
MSM: men who have sex with men

- Anal cancer in MSM is almost as high as cervical cancer prior to screening
- HIV-positive MSM are at higher risk of anal cancer

1. Palefsky JM J Adolesc Health. 2010 Apr; 46(4 Suppl): S12–S19.; 2. D'Souza G et al. J Acquir Immune Defic Syndr. 2008 Aug 1;48(4):491-9.; 3. Chin-Hong PV et al. Clin Infect Dis. 2002 Nov 1;35(9):1127-34.

HPV Vaccines in Canada

HPV bivalent Vaccine (2vHPV)[1,3]



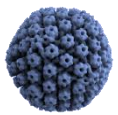
Females Only
9-45 years

HPV 9-valent Vaccine (9vHPV)[1,2]

Females & Males
9-45 years

Additional HPV Types Included in 9vHPV Vaccine

High-risk (cancer-causing) HPV genotypes



Low-risk (wart-causing) HPV genotypes

1. The National Advisory Committee on Immunization (NACI) Statement on HPV 2007-2017; 2. Gardasil Product Monograph. Merck Canada Inc.; 3. Cervarix Product Monograph. GlaxoSmithKline Inc.; 4. Gardasil 9 Product Monograph Merck Canada Inc.

Efficacy of 4vHPV Vaccine in Females 16-26 Years Old

Cancer **Prevention** Research

A Pooled Analysis of Continued Prophylactic Efficacy of Quadrivalent Human Papillomavirus (Types 6/11/16/18) Vaccine against High-grade Cervical and External Genital Lesions

Susanne K. Kjaer,[1] Kristján Sigurdsson,[2] Ole-Erik Iversen,[3] Mauricio Hernandez-Avila,[4] Cosette M. Wheeler,[5] Gonzalo Perez,[6] Darron R. Brown,[7] Laura A. Koutsky,[8] Eng Hseon Tay,[9] Patricia García,[10] Kevin A. Ault,[11] Suzanne M. Garland,[12] Sepp Leodolter,[13] Sven-Eric Olsson,[14] Grace W.K. Tang,[15] Daron G. Ferris,[16] Jorma Paavonen,[17] Matti Lehtinen,[18] Marc Steben,[19] F. Xavier Bosch,[20] Joakim Dillner,[21] Elmar A. Joura,[13] Slawomir Majewski,[22] Nubia Muñoz,[23] Evan R. Myers,[24] Luisa L. Villa,[25] Frank J. Taddeo,[26] Christine Roberts,[26] Amha Tadesse,[26] Janine Bryan,[26] Roger Maansson,[26] Shuang Lu,[26] Scott Vuocolo,[26] Teresa M. Hesley,[26] Alfred Saah,[26] Eliav Barr[26] and Richard M. Haupt[26]

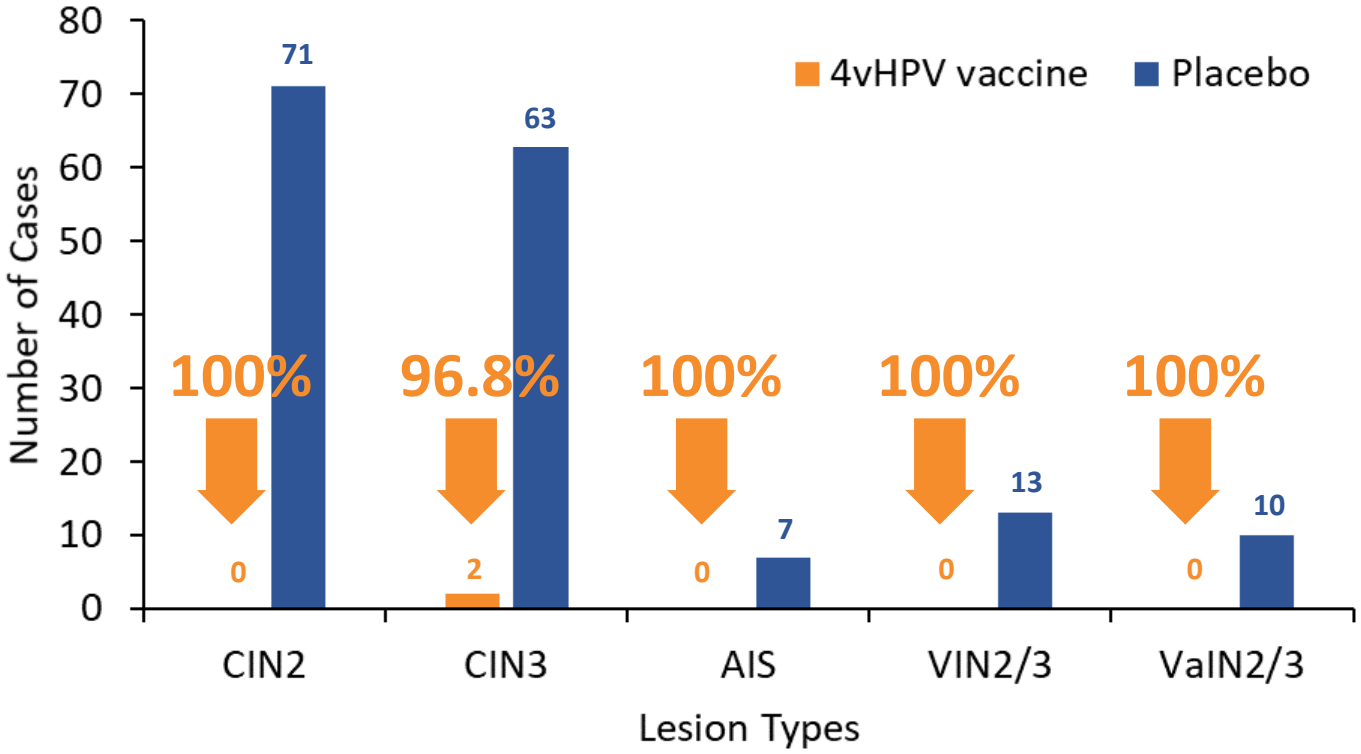
Abstract Quadrivalent human papillomavirus (HPV) vaccine has been shown to provide protection from HPV 6/11/16/18–related cervical, vaginal, and vulvar disease through 3 years. We provide an update on the efficacy of the quadrivalent HPV vaccine against high-grade cervical, vaginal, and vulvar lesions based on end-of-study data from three clinical trials. Additionally, we stratify vaccine efficacy by several baseline characteristics, including age, smoking status, and Papanicolaou (Pap) test results. A total of 18,174 females ages 16 to 26 years were randomized and allocated into one of three clinical trials (protocols 007, 013, and 015). Vaccine or placebo was given at baseline, month 2, and month 6. Pap testing was conducted at regular intervals. Cervical and anogenital swabs were collected for HPV DNA testing. Examination for the presence of vulvar and vaginal lesions was also done. Endpoints included high-grade cervical, vulvar, or vaginal lesions (CIN 2/3, VIN 2/3, or VaIN 2/3). Mean follow-up time was 42 months post dose 1. Vaccine efficacy against HPV 6/11/16/18–related high-grade cervical lesions in the per-protocol and intention-to-treat populations was 98.2% [95% confidence interval (95% CI), 93.3-99.8] and 51.5% (95% CI, 40.6-60.6), respectively. Vaccine efficacy against HPV 6/11/16/18–related high-grade vulvar and vaginal lesions in the per-protocol and intention-to-treat populations was 100.0% (95% CI, 82.6-100.0) and 79.0% (95% CI, 56.4-91.0), respectively. Efficacy in the intention-to-treat population tended to be lower in older women, women with more partners, and women with abnormal Pap test results. The efficacy of quadrivalent HPV vaccine against high-grade cervical and external anogenital neoplasia remains high through 42 months post vaccination.

Authors' Affiliations: [1]Department of Virus, Hormones and Cancer, Institute of Cancer Epidemiology, Danish Cancer Society/Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [2]National Cancer Detection Clinic, Reykjavik, Iceland; [3]Department of Clinical Medicine, University of Bergen and Department of Obstetrics and Gynecology, Haukeland University Hospital, Bergen, Norway; [4]Institute of Public Health, Cuernavaca, Morelos, Mexico; [5]Departments of Molecular Genetics and Microbiology and Obstetrics and Gynecology, University of New Mexico, Albuquerque, New Mexico; [6]Universidad del Rosario, Bogotá, Colombia; [7]Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana; [8]Department of Epidemiology, University of Washington, Seattle, Washington; [9]KK Women's & Children's Hospital, Singapore; [10]Epidemiology HIV and STD Unit, Universidad Peruana Cayetano Heredia, Lima, Peru; [11]Department of Gynecology and Obstetrics, Emory University School of Medicine, Atlanta, Georgia; [12]Microbiology and Infectious Diseases Department, Royal Women's Hospital and Department of Obstetrics and Gynecology, University of Melbourne, Melbourne, Victoria, Australia; [13]Department of Gynecology and Obstetrics, Medical University of Vienna, Vienna, Austria; [14]Karolinska Institute at Danderyd Hospital, Stockholm, Sweden; [15]Department of Obstetrics and Gynecology, University of Hong Kong, Hong Kong Special Administrative Region, China; [16]Department of Family Medicine and Obstetrics and Gynecology, Medical College of Georgia, Augusta, Georgia; [17]Department of Obstetrics and Gynecology, University Central Hospital, Helsinki, Finland; [18]School of Public Health, University of Tampere, Tampere, Finland; [19]Direction Risques Biologiques, Environnementaux et Occupationnels, Institut National de Santé Publique du Québec, Montreal, Québec, Canada; [20]Institut Catala d'Oncologia, IDIBELL, Barcelona, Spain; [21]Department of Medical Microbiology, Lund University, Lund, Sweden; [22]Department of Dermatology and Venereology, Center of Diagnostics and Treatment of Sexually Transmitted Diseases, Warsaw Medical University, Warsaw, Poland; [23]National Institute of Cancer, Bogotá, Colombia; [24]Department of Obstetrics and Gynecology, Duke University Medical Center, Durham, North Carolina; [25]Department of Virology, Ludwig Institute for Cancer Research, Sao Paulo, Brazil; and [26]Merck Research Laboratories, West Point, Pennsylvania

Requests for reprints: Susanne K. Kjaer, Department of Virus, Hormones and Cancer, Institute of Cancer Epidemiology, Danish Cancer Society/Rigshospitalet, Copenhagen, Denmark. Phone: 45-3525-7663; Fax: 45-3525-7683; E-mail: susanne@cancer.dk.

doi:10.1158/1940-6207.CAPR-09-0031

Vaccine Efficacy Against HPV 6/11/16/18-related High-grade Cervical, Vulvar and Vaginal Lesions (Per-protocol)



CIN: cervical intraepithelial neoplasias; VIN: vulvar intraepithelial neoplasias; VaIN: vaginal intraepithelial neoplasias; AIS: cervical adenocarcinoma *in situ*

Kjaer SK et al. Cancer Prev Res (Phila). 2009 Oct;2(10):868-78. .

Efficacy of 4vHPV Vaccine in Females 24-45 Years Old

British Journal of Cancer (2011) 105, 28–37
© 2011 Cancer Research UK All rights reserved 0007–0920/11
www.bjcancer.com

Clinical Studies

End-of-study safety, immunogenicity, and efficacy of quadrivalent HPV (types 6, 11, 16, 18) recombinant vaccine in adult women 24–45 years of age

X Castellsagué*,[1], N Muñoz[2], P Pitisuttithum[3], D Ferris[4], J Monsonego[5], K Auk[6], J Luna[2], E Myers[7], S Mallary[8], OM Bautista[8], J Bryan[8], S Vuocolo[8], RM Haupt[8] and A Saah[8]

[1]Unit of Infections and Cancer, Cancer Epidemiology Research Program, IDIBELL, Institut Català d'Oncologia-ICO, CIBER-ESP, L'Hospitalet de Llobregat, Catalonia 08907, Spain; [2]National Institute of Cancer, Bogotá, Colombia; [3]Faculty of Tropical Medicine, Vaccine Trial Center, Mahidol University, Bangkok, Thailand; [4]Departments of Family Medicine and Obstetrics and Gynecology, Medical College of Georgia, Augusta, GA, USA; [5]Department of Cyto-colposcopy, Fédération Mutualiste Parisienne, Paris, France; [6]Department of Gynecology and Obstetrics and the Emory Vaccine Center, Emory University School of Medicine, Atlanta, GA, USA; [7]Department of Obstetrics and Gynecology, Duke University Medical Center, Durham, NC, USA; [8]Merck & Co. Inc., North Wales, PA, USA

BACKGROUND: Previous analyses from a randomised trial in women aged 24–45 years have shown the quadrivalent human papillomavirus (qHPV) vaccine to be efficacious in the prevention of infection, cervical intraepithelial neoplasia (CIN), and external genital lesions (EGLs) related to HPV 6/11/16/18. In this report, we present end-of-study efficacy, safety, and immunogenicity data with a median follow-up time of 4.0 years.

METHODS: We enrolled 3819 24–45-year-old women with no history of cervical disease or genital warts in the past 5 years. Women received quadrivalent vaccine or placebo at day 1, and at months 2 and 6. Ascertainment of CIN/EGL was accomplished through Pap testing, genital inspection, and cervicovaginal sampling (every 6 months). The main analysis was conducted in a per-protocol efficacy population (that received three doses, was naive to the relevant HPV types at day 1, and remained free of infection through month 7). Efficacy was also estimated in other naive and non-naive populations.

RESULTS: Vaccine efficacy against the combined incidence of persistent infection, CIN/EGL related to HPV6/11/16/18 in the per-protocol population was 88.7% (95% CI: 78.1, 94.8). Efficacy for women who were seropositive and DNA negative for the relevant vaccine HPV type at the time of enrolment who received at least 1 dose was 66.9% (95% CI: 4.3, 90.6). At month 48, 91.5, 92.0, 97.4, and 47.9% of vaccinated women were seropositive to HPV 6/11/16/18, respectively. No serious vaccine-related adverse experiences were reported.

CONCLUSIONS: The qHPV vaccine demonstrated high efficacy, immunogenicity, and acceptable safety in women aged 24–45 years, regardless of previous exposure to HPV vaccine type.

British Journal of Cancer (2011) 105, 28–37. doi:10.1038/bjc.2011.185 www.bjcancer.com
Published online 31 May 2011

Keywords: HPV; vaccine; cervical; adult

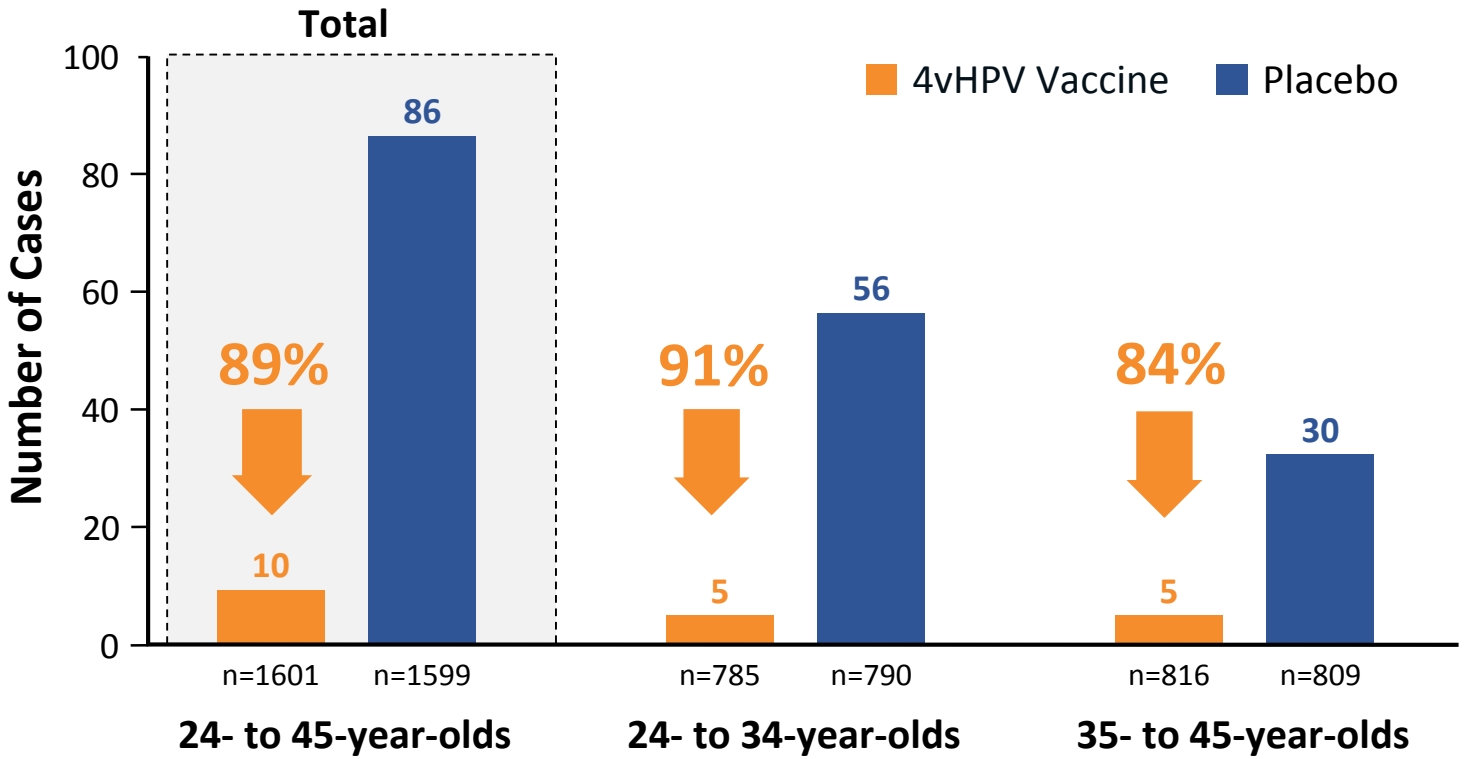
Persistent infection of the uterine cervix by 15–20 carcinogenic human papillomavirus (HPV) genotypes leads to the vast majority of cervical cancers (Walboomers *et al*, 1999; Muñoz *et al*, 2003) and related precursor lesions (International Agency for Research on Cancer Working Group, 2007). Although most sexually active women are at risk of HPV infection, the incidence of HPV infection peaks soon after the onset of sexual activity in most populations (Jacobs *et al*, 2000; Schiffman and Kjaer, 2003; Dunne *et al*, 2007). Although incidence rates tend to decline thereafter, women older than age 25 years also remain at risk for acquisition of new HPV infections (Castellsague *et al*, 2009; Munoz *et al*, 2009).

Data from Colombia show that the 5-year cumulative risk of incident cervical HPV infection decreased from 42.5% in females aged 15–19 years to 30% in those aged 25–29 years, and to 22% in those aged 30–44 years (Munoz *et al*, 2004). However, a second peak in HPV DNA prevalence has been observed in women in the fourth and fifth decades of life (de Sanjose *et al*, 2007). Whether this second peak is due to new infections, viral reactivation, waning immunity, or another mechanism is unclear. The cohort study from Colombia supports the possibility of new infections, as the curve of incident high-risk HPV infections is also bimodal with a first peak in women under 25 years of age and a second peak after menopause (Munoz *et al*, 2004). Conflicting evidence with respect to a bimodal infection peak is provided byRodriguez *et al* (2010), although these two studies are not directly comparable.

Previous studies have demonstrated that the prophylactic quadrivalent HPV (qHPV) vaccine is highly effective in preventing HPV 6-, 11-, 16-, or 18-related high-grade cervical, vulvar, or vaginal intraepithelial neoplasia (CIN, VIN, or VaIN, respectively),

*Correspondence: Dr X Castellsagué; E-mail: xcastellsague@iconcologia.net or castellsagues@gmail.com
Received 3 February 2011; revised 18 April 2011; accepted 26 April 2011; published online 31 May 2011

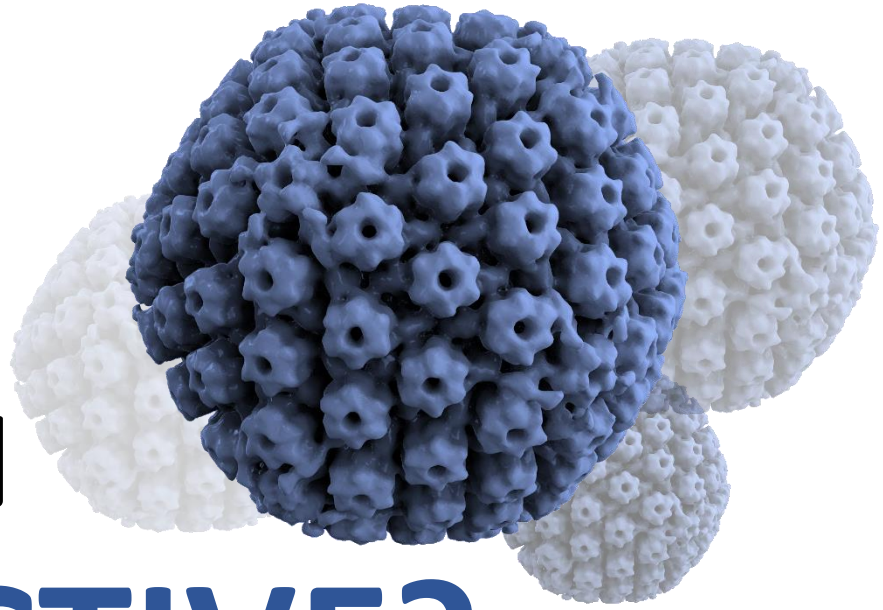
Vaccine Efficacy Against HPV 6/11/16/18-related Persistent Infection, CIN (Any Grade), and EGL (Per-protocol)



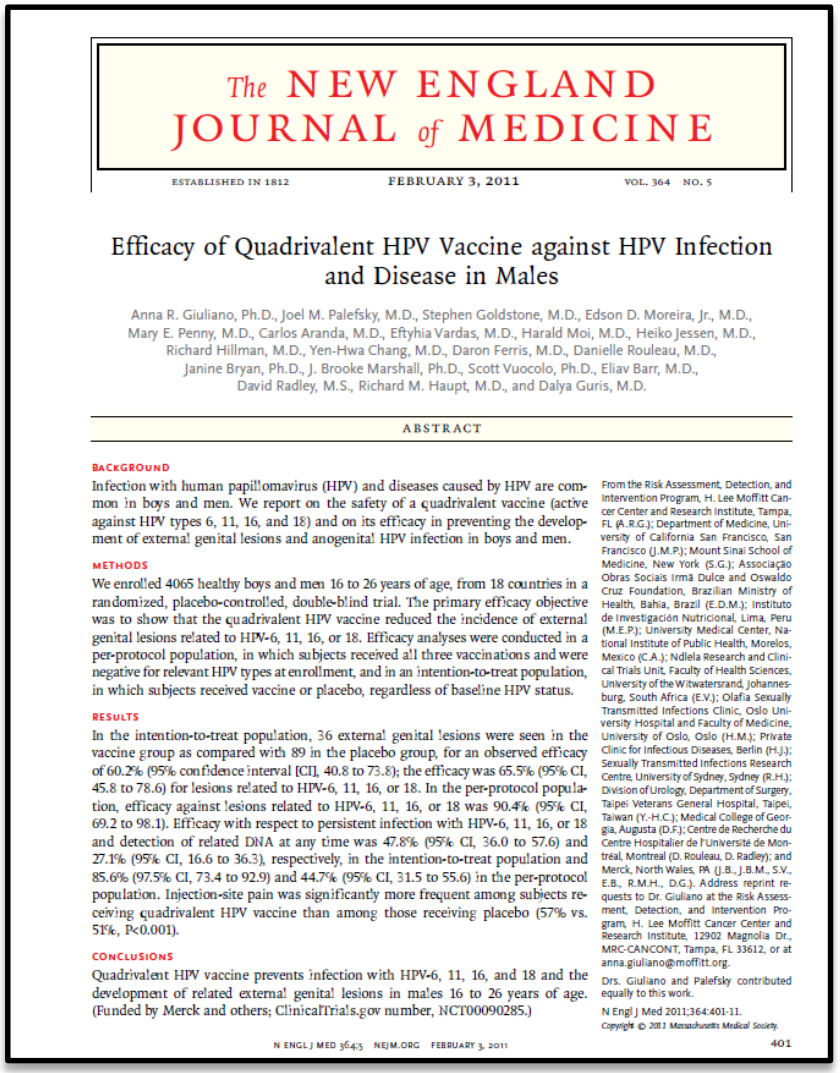
CIN: cervical intraepithelial neoplasias; EGL: external genital lesions

Castellagué X et al. Br J Cancer. 2011 Jun 28;105(1):28-37.

IS HPV VACCINATION IN MALES EFFECTIVE?



4vHPV Vaccine Reduces External Genital Lesions in Males 16-26 Years Old



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 3, 2011 VOL. 364 NO. 5

Efficacy of Quadrivalent HPV Vaccine against HPV Infection and Disease in Males

Anna R. Giuliano, Ph.D., Joel M. Palefsky, M.D., Stephen Goldstone, M.D., Edson D. Moreira, Jr., M.D., Mary E. Penny, M.D., Carlos Aranda, M.D., Eftyhia Vardas, M.D., Harald Moi, M.D., Heiko Jessen, M.D., Richard Hillman, M.D., Yen-Hwa Chang, M.D., Daron Ferris, M.D., Danielle Rouleau, M.D., Janine Bryan, Ph.D., J. Brooke Marshall, Ph.D., Scott Vuocolo, Ph.D., Eliav Barr, M.D., David Radley, M.S., Richard M. Haupt, M.D., and Dalya Guris, M.D.

ABSTRACT

BACKGROUND

Infection with human papillomavirus (HPV) and diseases caused by HPV are common in boys and men. We report on the safety of a quadrivalent vaccine (active against HPV types 6, 11, 16, and 18) and on its efficacy in preventing the development of external genital lesions and anogenital HPV infection in boys and men.

METHODS

We enrolled 4065 healthy boys and men 16 to 26 years of age, from 18 countries in a randomized, placebo-controlled, double-blind trial. The primary efficacy objective was to show that the quadrivalent HPV vaccine reduced the incidence of external genital lesions related to HPV-6, 11, 16, or 18. Efficacy analyses were conducted in a per-protocol population, in which subjects received all three vaccinations and were negative for relevant HPV types at enrollment, and in an intention-to-treat population, in which subjects received vaccine or placebo, regardless of baseline HPV status.

RESULTS

In the intention-to-treat population, 36 external genital lesions were seen in the vaccine group as compared with 89 in the placebo group, for an observed efficacy of 60.2% (95% confidence interval [CI], 40.8 to 73.8); the efficacy was 65.5% (95% CI, 45.8 to 78.6) for lesions related to HPV-6, 11, 16, or 18. In the per-protocol population, efficacy against lesions related to HPV-6, 11, 16, or 18 was 90.4% (95% CI, 69.2 to 98.1). Efficacy with respect to persistent infection with HPV-6, 11, 16, or 18 and detection of related DNA at any time was 47.8% (95% CI, 36.0 to 57.6) and 27.1% (95% CI, 16.6 to 36.3), respectively, in the intention-to-treat population and 85.6% (97.5% CI, 73.4 to 92.9) and 44.7% (95% CI, 31.5 to 55.6) in the per-protocol population. Injection-site pain was significantly more frequent among subjects receiving quadrivalent HPV vaccine than among those receiving placebo (57% vs. 51%, P<0.001).

CONCLUSIONS

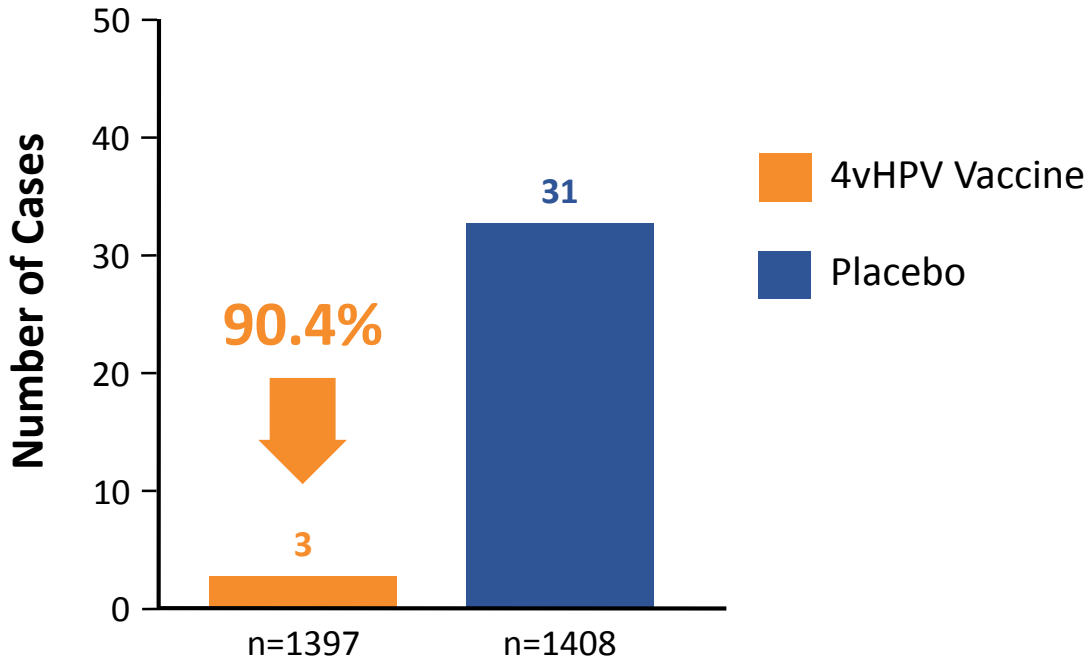
Quadrivalent HPV vaccine prevents infection with HPV-6, 11, 16, and 18 and the development of related external genital lesions in males 16 to 26 years of age. (Funded by Merck and others; ClinicalTrials.gov number, NCT00090285.)

From the Risk Assessment, Detection, and Intervention Program, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL (A.R.G.); Department of Medicine, University of California San Francisco, San Francisco (J.M.P.); Mount Sinai School of Medicine, New York (S.G.); Associação Obras Sociais Irmã Dulce and Oswaldo Cruz Foundation, Brazilian Ministry of Health, Bahia, Brazil (E.D.M.); Instituto de Investigación Nutricional, Lima, Peru (M.E.P.); University Medical Center, National Institute of Public Health, Morelos, Mexico (C.A.); Ndlela Research and Clinical Trials Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa (E.V.); Olafia Sexually Transmitted Infections Clinic, Oslo University Hospital and Faculty of Medicine, University of Oslo, Oslo (H.M.); Private Clinic for Infectious Diseases, Berlin (H.J.); Sexually Transmitted Infections Research Centre, University of Sydney, Sydney (R.H.); Division of Urology, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan (Y.-H.C.); Medical College of Georgia, Augusta (D.F.); Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Montreal (D. Rouleau, D. Radley); and Merck, North Wales, PA (J.B., J.B.M., S.V., E.B., R.M.H., D.G.). Address reprint requests to Dr. Giuliano at the Risk Assessment, Detection, and Intervention Program, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Dr., MRC-CANCONT, Tampa, FL 33612, or at anna.giuliano@moffitt.org.

Drs. Giuliano and Palefsky contributed equally to this work.

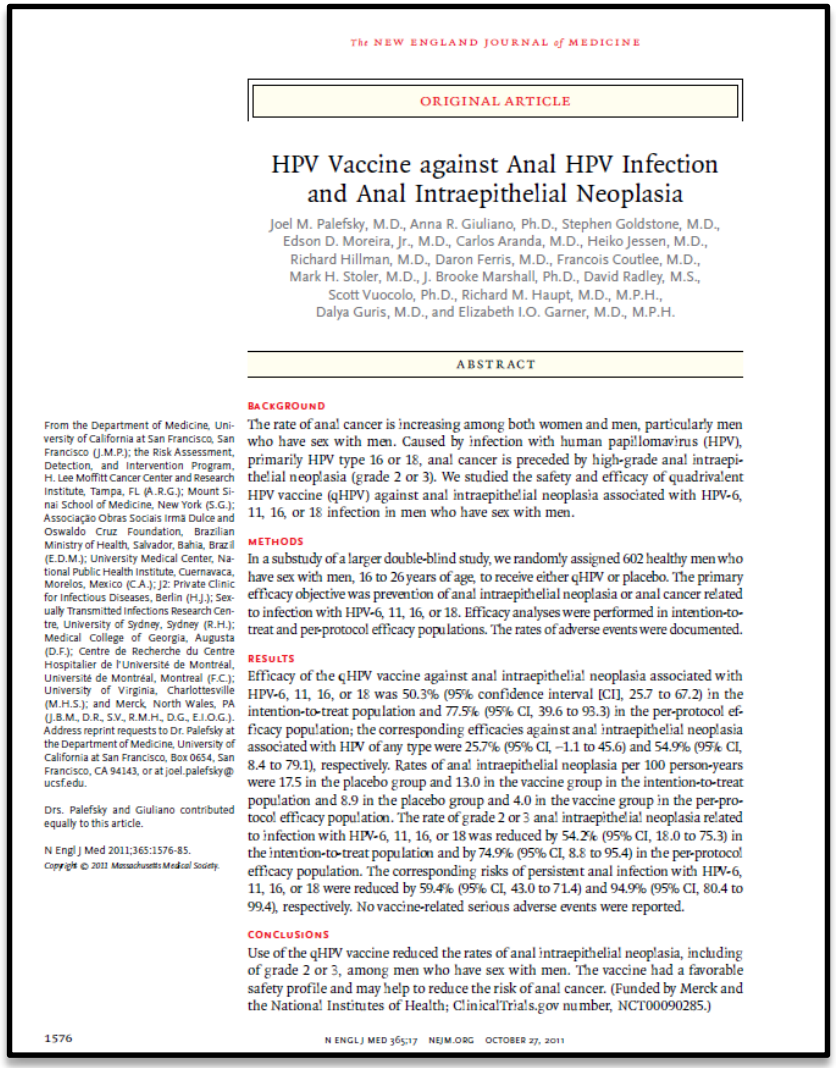
N Engl J Med 2011;364:401-11.

Vaccine Efficacy Against HPV 6/11/16/18-related External Genital Lesions (Per-protocol)



Giuliano AR et al. N Engl J Med. 2011 Feb 3;364(5):401-11.

4vHPV Vaccine Reduces Anal Neoplasia in Males 16-26 Years Old



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

HPV Vaccine against Anal HPV Infection and Anal Intraepithelial Neoplasia

Joel M. Palefsky, M.D., Anna R. Giuliano, Ph.D., Stephen Goldstone, M.D., Edson D. Moreira, Jr., M.D., Carlos Aranda, M.D., Heiko Jessen, M.D., Richard Hillman, M.D., Daron Ferris, M.D., Francois Coutlee, M.D., Mark H. Stoler, M.D., J. Brooke Marshall, Ph.D., David Radley, M.S., Scott Vuocolo, Ph.D., Richard M. Haupt, M.D., M.P.H., Dalya Guris, M.D., and Elizabeth I.O. Garner, M.D., M.P.H.

ABSTRACT

BACKGROUND

The rate of anal cancer is increasing among both women and men, particularly men who have sex with men. Caused by infection with human papillomavirus (HPV), primarily HPV type 16 or 18, anal cancer is preceded by high-grade anal intraepithelial neoplasia (grade 2 or 3). We studied the safety and efficacy of quadrivalent HPV vaccine (qHPV) against anal intraepithelial neoplasia associated with HPV-6, 11, 16, or 18 infection in men who have sex with men.

METHODS

In a substudy of a larger double-blind study, we randomly assigned 602 healthy men who have sex with men, 16 to 26 years of age, to receive either qHPV or placebo. The primary efficacy objective was prevention of anal intraepithelial neoplasia or anal cancer related to infection with HPV-6, 11, 16, or 18. Efficacy analyses were performed in intention-to-treat and per-protocol efficacy populations. The rates of adverse events were documented.

RESULTS

Efficacy of the qHPV vaccine against anal intraepithelial neoplasia associated with HPV-6, 11, 16, or 18 was 50.3% (95% confidence interval [CI], 25.7 to 67.2) in the intention-to-treat population and 77.5% (95% CI, 39.6 to 93.3) in the per-protocol efficacy population; the corresponding efficacies against anal intraepithelial neoplasia associated with HPV of any type were 25.7% (95% CI, −1.1 to 45.6) and 54.9% (95% CI, 8.4 to 79.1), respectively. Rates of anal intraepithelial neoplasia per 100 person-years were 17.5 in the placebo group and 13.0 in the vaccine group in the intention-to-treat population and 8.9 in the placebo group and 4.0 in the vaccine group in the per-protocol efficacy population. The rate of grade 2 or 3 anal intraepithelial neoplasia related to infection with HPV-6, 11, 16, or 18 was reduced by 54.2% (95% CI, 18.0 to 75.3) in the intention-to-treat population and by 74.9% (95% CI, 8.8 to 95.4) in the per-protocol efficacy population. The corresponding risks of persistent anal infection with HPV-6, 11, 16, or 18 were reduced by 59.4% (95% CI, 43.0 to 71.4) and 94.9% (95% CI, 80.4 to 99.4), respectively. No vaccine-related serious adverse events were reported.

CONCLUSIONS

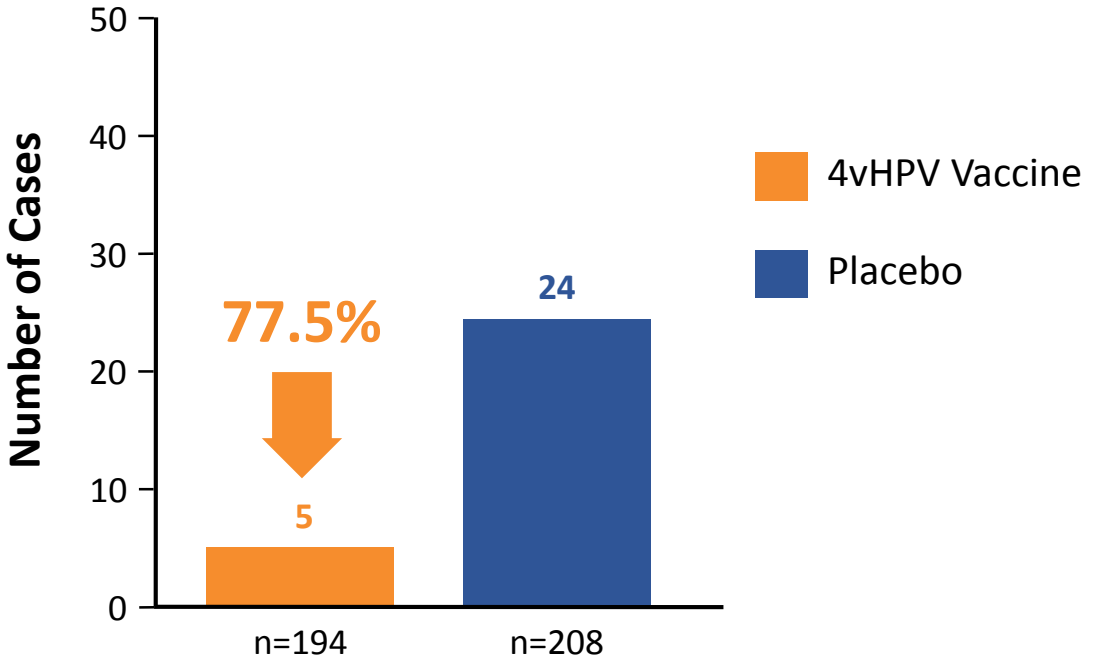
Use of the qHPV vaccine reduced the rates of anal intraepithelial neoplasia, including of grade 2 or 3, among men who have sex with men. The vaccine had a favorable safety profile and may help to reduce the risk of anal cancer. (Funded by Merck and the National Institutes of Health; ClinicalTrials.gov number, NCT00090285.)

From the Department of Medicine, University of California at San Francisco, San Francisco (J.M.P.); the Risk Assessment, Detection, and Intervention Program, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL (A.R.G.); Mount Sinai School of Medicine, New York (S.G.); Associação Obras Sociais Irmã Dulce and Oswaldo Cruz Foundation, Brazilian Ministry of Health, Salvador, Bahia, Brazil (E.D.M.); University Medical Center, National Public Health Institute, Cuernavaca, Morelos, Mexico (C.A.); J2: Private Clinic for Infectious Diseases, Berlin (H.J.); Sexually Transmitted Infections Research Centre, University of Sydney, Sydney (R.H.); Medical College of Georgia, Augusta (D.F.); Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Université de Montréal, Montreal (F.C.); University of Virginia, Charlottesville (M.H.S.); and Merck, North Wales, PA (J.B.M., D.R., S.V., R.M.H., D.G., E.I.O.G.). Address reprint requests to Dr. Palefsky at the Department of Medicine, University of California at San Francisco, Box 0654, San Francisco, CA 94143, or at joel.palefsky@ucsf.edu.

Drs. Palefsky and Giuliano contributed equally to this article.

N Engl J Med 2011;365:1576-85.

Vaccine Efficacy Against HPV 6/11/16/18-related Anal Neoplasia in MSM (Per-protocol)



n = number of subjects who have at least 1 follow-up visit after month 7
MSM: men who have sex with men

Palefsky JM et al. N Engl J Med. 2011 Oct 27;365(17):1576-85.

4vHPV Vaccine is Safe and Immunogenic in Males 27-45 Years Old

Vaccine 33 (2015) 5640–5646

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Immunogenicity and safety of Gardasil among mid-adult aged men (27–45 years)—The MAM Study

Anna R. Giuliano[a,*], Kimberly Isaacs-Soriano[a], B. Nelson Torres[a], Martha Abrahamsen[a], Donna J. Ingles[a], Bradley A. Sirak[a], Manuel Quiterio[b], Eduardo Lazcano-Ponce[b]

[a] Center for Infection Research in Cancer, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, Tampa, FL 33612, United States
[b] Instituto Nacional de Salud Publica, Av. Universidad 655, Col. Santa Maria Ahuacatitlan, 62508 Cuernavaca, MOR, Mexico

ARTICLE INFO

Article history:
Received 1 July 2015
Received in revised form 24 August 2015
Accepted 25 August 2015
Available online 4 September 2015

Clinical trial registration number:
NCT01432574

Keywords:
Human papillomavirus
HPV
Vaccine
Mid-adult men

ABSTRACT

Background: The quadrivalent (types 6/11/16/18) human papillomavirus (HPV) vaccine, Gardasil, has demonstrated efficacy against persistent HPV infection and associated anogenital disease in males. The goal of this Phase II trial was to establish the immunogenicity and safety of Gardasil among mid-adult men ages 27–45 years.
Methods: One hundred and fifty men from Tampa, FL, US, and Cuernavaca, Mexico who met eligibility criteria (male, 27–45 years old, completed four years of follow-up in the HPV Infection in Men (HIM) natural history study) were enrolled. Subjects completed four visits over seven months, with Gardasil administered at Day 1 and Months 2 and 6. Sera were collected at Day 1 (pre-vaccination) and Month 7 (one month post-dose three). Anti-HPV6, 11, 16, and 18 IgG levels were determined by competitive Luminex immunoassay.
Findings: 100% of men seroconverted to each of the four HPV vaccine components, and the vaccine was generally well-tolerated. Antibody responses to vaccine did not differ by age group or sexual orientation, regardless of HPV type, and were significantly higher at Month 7 among men who entered the trial seropositive for HPV 6 or 11.
Interpretation: The immune response to HPV vaccination in men ages 27–45 was comparable to that observed in younger men, in whom clinical efficacy was demonstrated. Further trials to assess the efficacy of HPV vaccines to prevent persistent HPV infections in mid-adult men are needed.
Funding: Merck & Co. Inc. was the main sponsor of this trial (IISP39256) and provided the study product.

1. Introduction

Human papillomavirus (HPV) infects the squamous epithelium of both genders, leading to anogenital condyloma acuminata and cancers of the penis, anus, and oropharynx in men [1]. In any 12-month period, the probability of a sexually active man acquiring a new genital HPV infection is 0.29–0.39 per 1000 person-months [2–4], comparable to estimates reported for women. However, unlike women, the rate of acquisition of new genital HPV infections in men remains constant with increasing age [5]. Correspondingly, an older median age at diagnosis of HPV-related cancers is observed in men compared to women. Underlying these differences by gender in HPV natural history with age may be differences in the immune response to natural HPV infection between the sexes. The proportion of men who are HPV seropositive is lower than that reported in women [5]. Among men and women who are HPV seropositive, antibody titers are higher in women compared to men, and antibodies to natural infection do not appear to provide protection against subsequent HPV infection in men, while partial protection is noted among women [6,7]. This lower immune response to natural infection may partially explain the overall higher prevalence of HPV infections observed in men and the sustained incidence and prevalence of HPV infection at multiple anatomic sites (anal, genital, oral) observed across the lifespan of men.

HPV vaccination may be the only reliable method to provide protection against new HPV infections in men. As previously shown, the quadrivalent HPV (types 6/11/16/18) vaccine, Gardasil, was efficacious in preventing persistent anogenital HPV infection and external genital lesions caused by HPV 6/11/16/18 in men ages 16–26 years [8]. No previous studies have assessed whether healthy mid-adult aged men, those who are at higher risk of HPV-related

* Corresponding author. Tel.: +1 813 745 6820; fax: +1 813 745 5606.
E-mail address: Anna.Giuliano@moffitt.org (A.R. Giuliano).

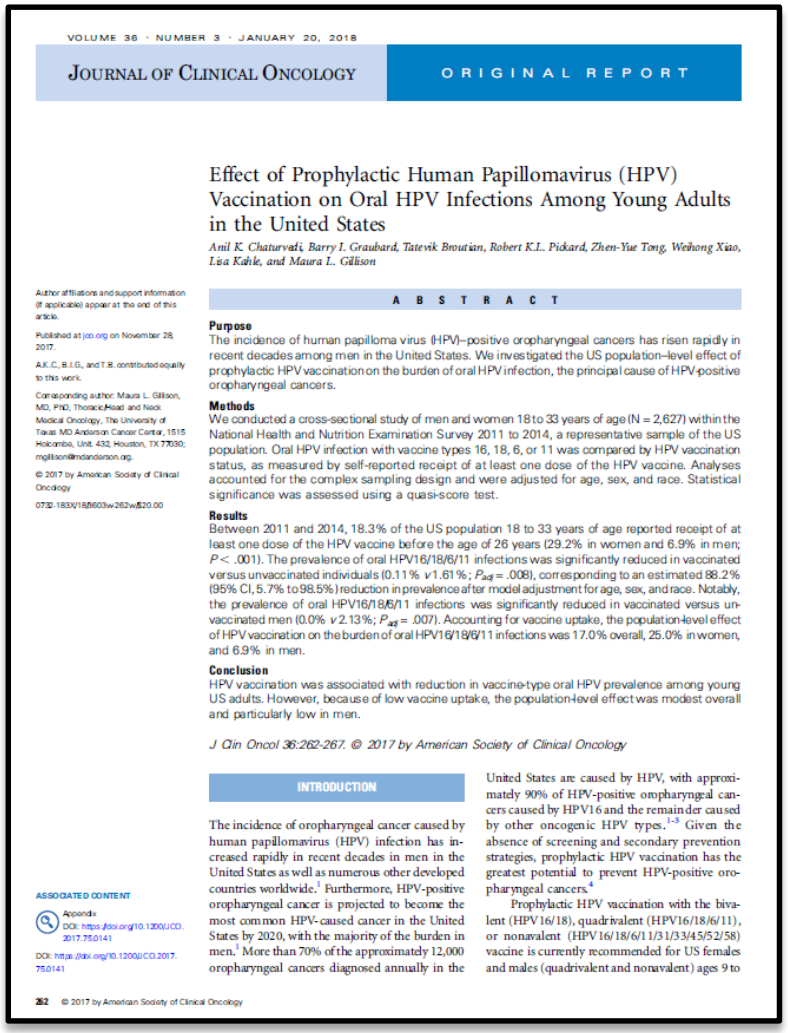
http://dx.doi.org/10.1016/j.vaccine.2015.08.072
0264-410X/

100% of males **27 to 45 years** of age vaccinated with 4vHPV vaccine in the Mid-Adult Aged Men (MAM) study seroconverted at month 7

HPV Types	n	Seropositive (%)
HPV 6	145	100.0
HPV 11	145	100.0
HPV 16	145	100.0
HPV 18	145	100.0

Giuliano AR et al. Vaccine. 2015 Oct 13;33(42):5640-5646.

Decline of Oral HPV Infections Among US Adults 18-33 Years Old Post-Vaccination



VOLUME 36 · NUMBER 3 · JANUARY 20, 2018

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Effect of Prophylactic Human Papillomavirus (HPV) Vaccination on Oral HPV Infections Among Young Adults in the United States

Anil K. Chaturvedi, Barry I. Graubard, Tatevik Broutian, Robert K.L. Pickard, Zhen-Yue Tong, Weihong Xiao, Lisa Kahle, and Maura L. Gillison

Author affiliations and support information (if applicable) appear at the end of this article.

Published at jco.org on November 28, 2017.

A.K.C., B.I.G., and T.B. contributed equally to this work.

Corresponding author: Maura L. Gillison, MD, PhD, Thoracic/Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center, 1515 Holcombe, Unit 432, Houston, TX 77030; mgillison@mdanderson.org.

0732-183X/18/3603w-262w/$20.00

ABSTRACT

Purpose
The incidence of human papilloma virus (HPV)–positive oropharyngeal cancers has risen rapidly in recent decades among men in the United States. We investigated the US population–level effect of prophylactic HPV vaccination on the burden of oral HPV infection, the principal cause of HPV-positive oropharyngeal cancers.

Methods
We conducted a cross-sectional study of men and women 18 to 33 years of age (N = 2,627) within the National Health and Nutrition Examination Survey 2011 to 2014, a representative sample of the US population. Oral HPV infection with vaccine types 16, 18, 6, or 11 was compared by HPV vaccination status, as measured by self-reported receipt of at least one dose of the HPV vaccine. Analyses accounted for the complex sampling design and were adjusted for age, sex, and race. Statistical significance was assessed using a quasi-score test.

Results
Between 2011 and 2014, 18.3% of the US population 18 to 33 years of age reported receipt of at least one dose of the HPV vaccine before the age of 26 years (29.2% in women and 6.9% in men; $P < .001$). The prevalence of oral HPV16/18/6/11 infections was significantly reduced in vaccinated versus unvaccinated individuals (0.11% *v* 1.61%; $P_{adj} = .008$), corresponding to an estimated 88.2% (95% CI, 5.7% to 98.5%) reduction in prevalence after model adjustment for age, sex, and race. Notably, the prevalence of oral HPV16/18/6/11 infections was significantly reduced in vaccinated versus unvaccinated men (0.0% *v* 2.13%; $P_{adj} = .007$). Accounting for vaccine uptake, the population-level effect of HPV vaccination on the burden of oral HPV16/18/6/11 infections was 17.0% overall, 25.0% in women, and 6.9% in men.

Conclusion
HPV vaccination was associated with reduction in vaccine-type oral HPV prevalence among young US adults. However, because of low vaccine uptake, the population-level effect was modest overall and particularly low in men.

J Clin Oncol 36:262-267. © 2017 by American Society of Clinical Oncology

INTRODUCTION

The incidence of oropharyngeal cancer caused by human papillomavirus (HPV) infection has increased rapidly in recent decades in men in the United States as well as numerous other developed countries worldwide.[1] Furthermore, HPV-positive oropharyngeal cancer is projected to become the most common HPV-caused cancer in the United States by 2020, with the majority of the burden in men.[1] More than 70% of the approximately 12,000 oropharyngeal cancers diagnosed annually in the United States are caused by HPV, with approximately 90% of HPV-positive oropharyngeal cancers caused by HPV16 and the remainder caused by other oncogenic HPV types.[1-3] Given the absence of screening and secondary prevention strategies, prophylactic HPV vaccination has the greatest potential to prevent HPV-positive oropharyngeal cancers.[4]

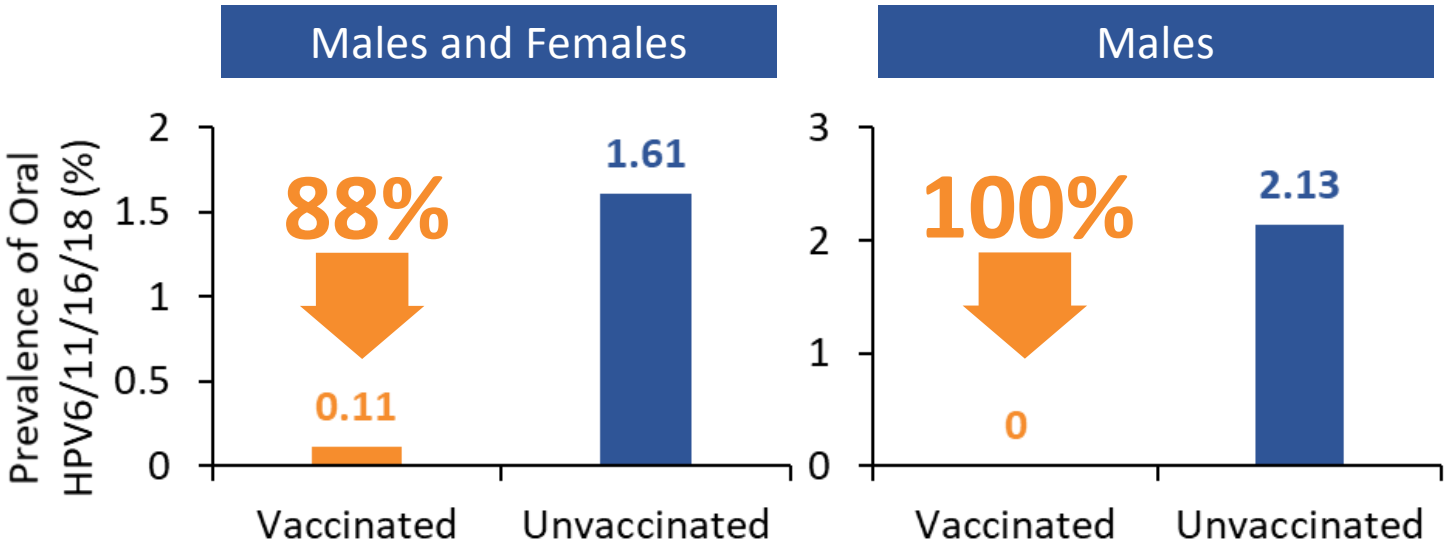
Prophylactic HPV vaccination with the bivalent (HPV16/18), quadrivalent (HPV16/18/6/11), or nonavalent (HPV16/18/6/11/31/33/45/52/58) vaccine is currently recommended for US females and males (quadrivalent and nonavalent) ages 9 to

ASSOCIATED CONTENT

Appendix

DOI: https://doi.org/10.1200/JCO.2017.75.0141

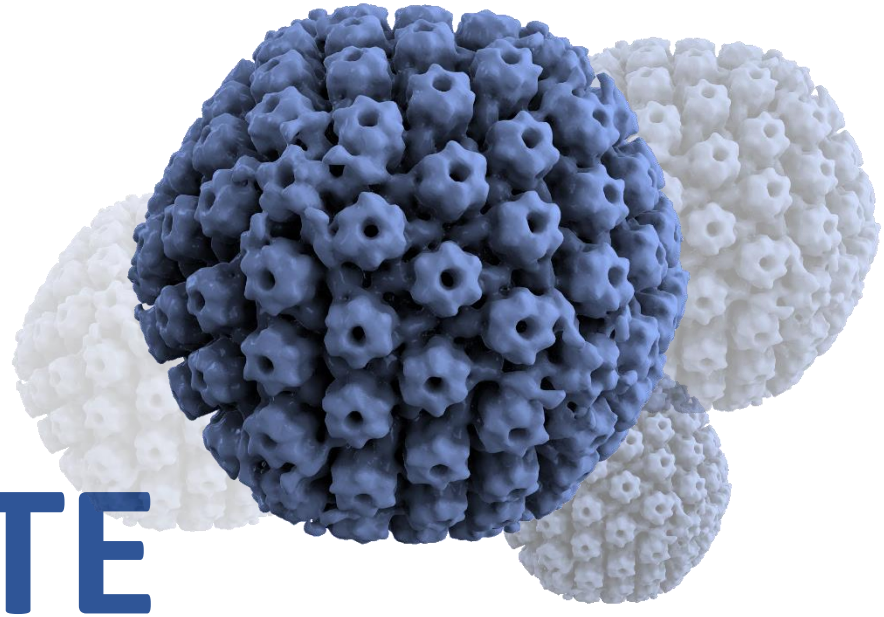
DOI: https://doi.org/10.1200/JCO.2017.75.0141



Currently no HPV vaccines outside of the US are approved for the prevention of oropharyngeal cancer and other head & neck cancers caused by HPV types 16, 18, 33, 45, 52, and 58.

Chaturvedi AK, Graubard BI, Broutian T, et al. J Clin Oncol. 2018 Jan 20;36(3):262-267. https://www.ncbi.nlm.nih.gov/pubmed/29182497

Males and Females with
Previous HPV Infections &
HPV-related disease



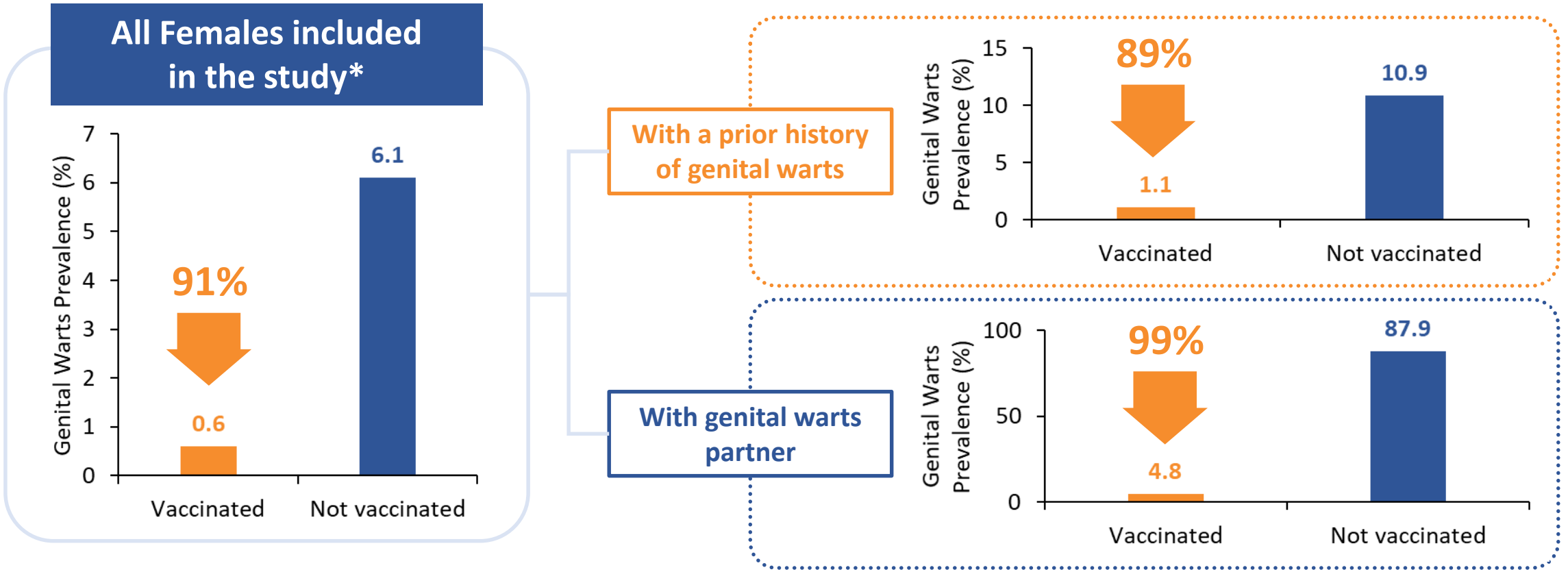
IS IT TOO LATE

Do They Still

BENEFIT FROM ?

HPV Vaccination

4vHPV Vaccination Reduces Genital Warts Prevalence and Recurrence in Females



*Prevalences were caculated based on genital warts episodes recorded at least one year after immunization. Petráš M, Adámková V. Vaccine. 2015 Nov 17;33(46):6264-7.

4vHPV Vaccination After Treatment Reduces Risk of CIN2+ Recurrence

Systematic Review & Meta-Analysis on 10 Studies

Independent from HPV Types

59%

Risk Reduction of recurrent CIN2+ After HPV Vaccination

RR=0.41
95% CI [0.27; 0.64]

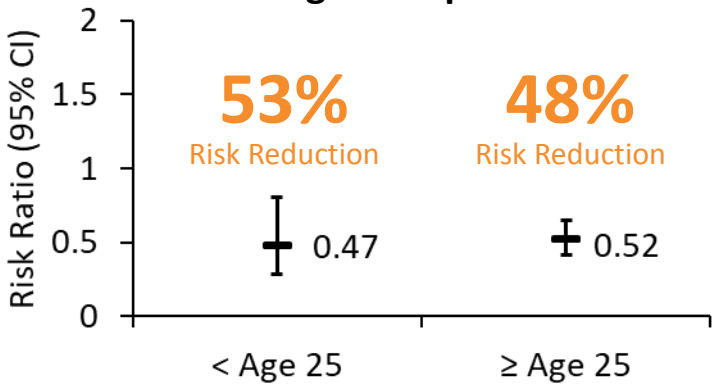
HPV 16/18-related

63%

Risk Reduction of recurrent CIN2+ After HPV Vaccination

RR=0.37;
95% CI [0.17; 0.80]

Risk Reduction Did not Vary Across Different Age Groups



Risk of recurrent CIN2+ was significantly reduced after surgical excision and HPV vaccination compared to surgical excision only

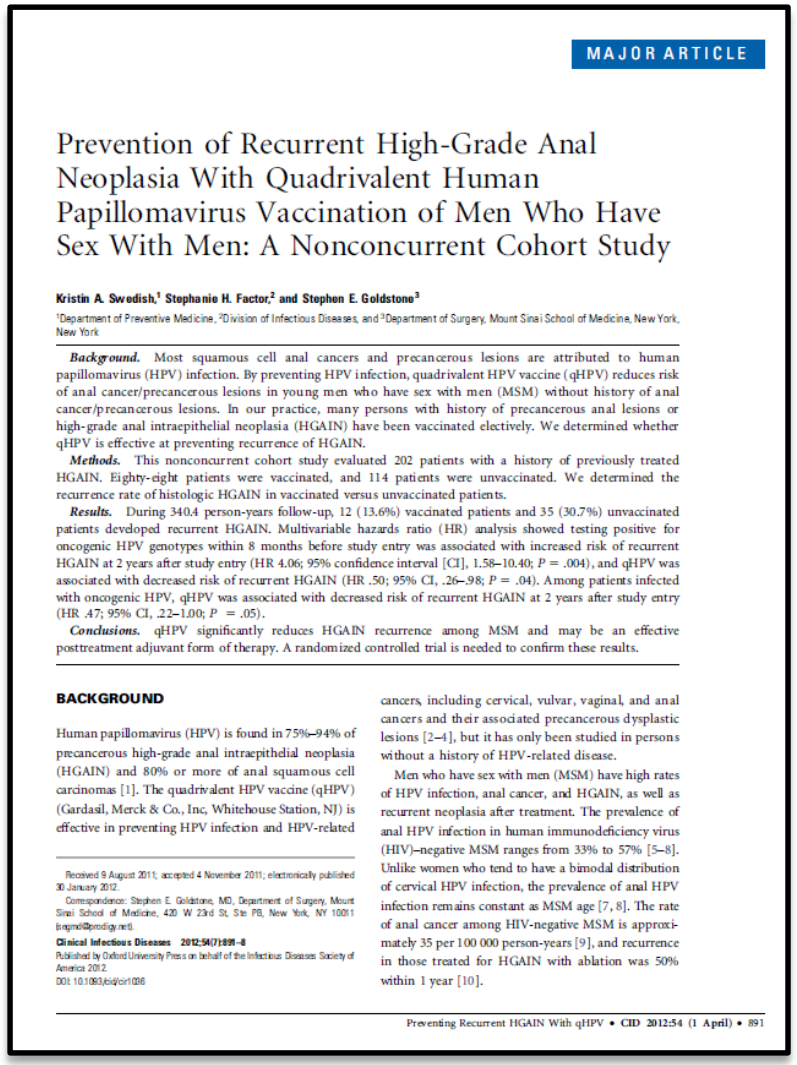
Jentschke M et al. *Vaccine*. 2020 Aug 4:S0264-410X(20)30986-5.

Recurrence of HPV-Related Diseases is High

Disease	Recurrence Rate
EGW	>40%
CIN 2+	>10%
HG-AIN	>30%
HG-AIN in MSM	>60%
HG-AIN in HIV+	>90%

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.

4vHPV Vaccination Reduces Recurrent High-Grade Anal Neoplasia in MSM



MAJOR ARTICLE

Prevention of Recurrent High-Grade Anal Neoplasia With Quadrivalent Human Papillomavirus Vaccination of Men Who Have Sex With Men: A Nonconcurrent Cohort Study

Kristin A. Swedish,[1] Stephanie H. Factor,[2] and Stephen E. Goldstone[3]

[1]Department of Preventive Medicine, [2]Division of Infectious Diseases, and [3]Department of Surgery, Mount Sinai School of Medicine, New York, New York

Background. Most squamous cell anal cancers and precancerous lesions are attributed to human papillomavirus (HPV) infection. By preventing HPV infection, quadrivalent HPV vaccine (qHPV) reduces risk of anal cancer/precancerous lesions in young men who have sex with men (MSM) without history of anal cancer/precancerous lesions. In our practice, many persons with history of precancerous anal lesions or high-grade anal intraepithelial neoplasia (HGAIN) have been vaccinated electively. We determined whether qHPV is effective at preventing recurrence of HGAIN.

Methods. This nonconcurrent cohort study evaluated 202 patients with a history of previously treated HGAIN. Eighty-eight patients were vaccinated, and 114 patients were unvaccinated. We determined the recurrence rate of histologic HGAIN in vaccinated versus unvaccinated patients.

Results. During 340.4 person-years follow-up, 12 (13.6%) vaccinated patients and 35 (30.7%) unvaccinated patients developed recurrent HGAIN. Multivariable hazards ratio (HR) analysis showed testing positive for oncogenic HPV genotypes within 8 months before study entry was associated with increased risk of recurrent HGAIN at 2 years after study entry (HR 4.06; 95% confidence interval [CI], 1.58–10.40; $P = .004$), and qHPV was associated with decreased risk of recurrent HGAIN (HR .50; 95% CI, .26–.98; $P = .04$). Among patients infected with oncogenic HPV, qHPV was associated with decreased risk of recurrent HGAIN at 2 years after study entry (HR .47; 95% CI, .22–1.00; $P = .05$).

Conclusions. qHPV significantly reduces HGAIN recurrence among MSM and may be an effective posttreatment adjuvant form of therapy. A randomized controlled trial is needed to confirm these results.

BACKGROUND

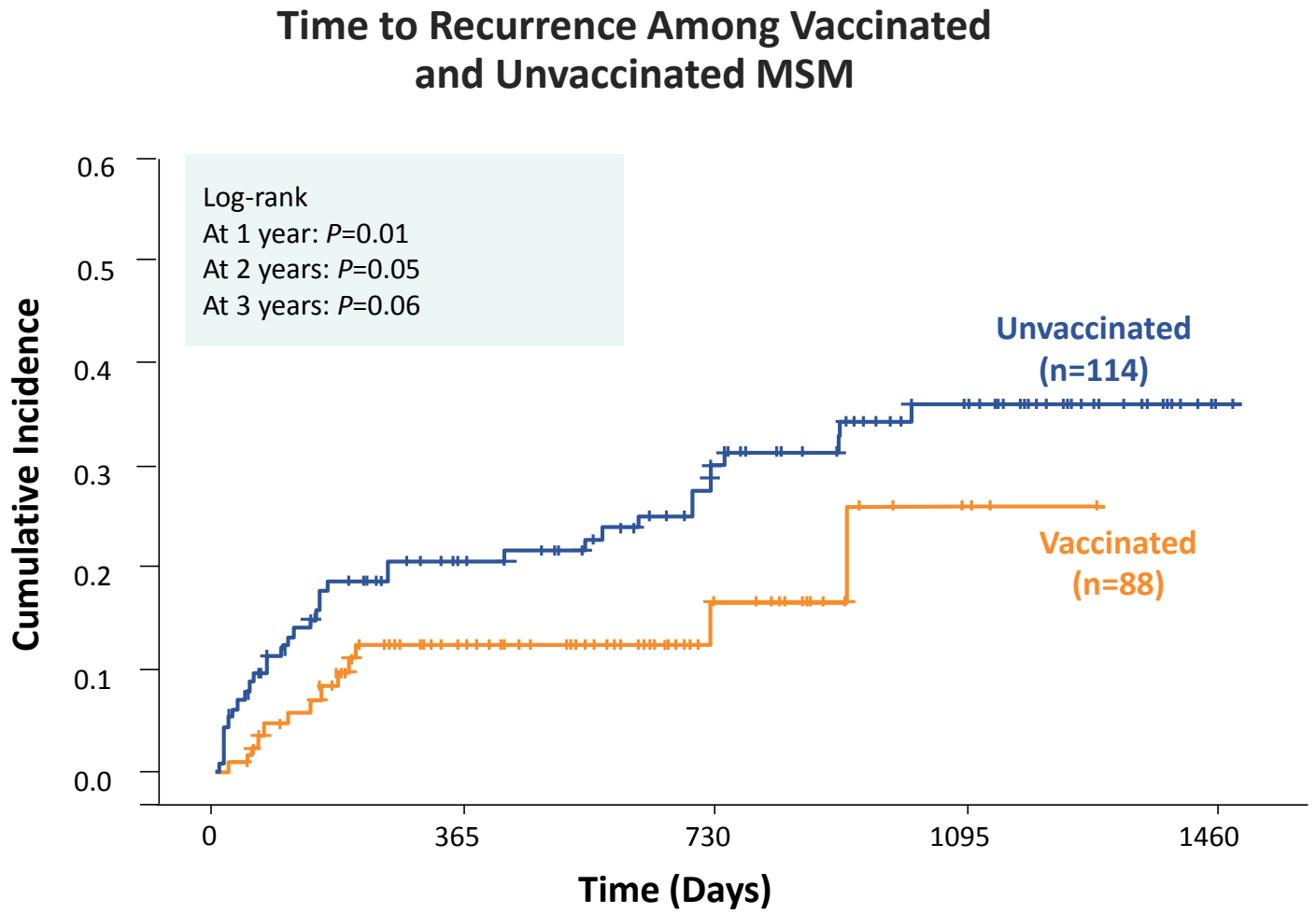
Human papillomavirus (HPV) is found in 75%–94% of precancerous high-grade anal intraepithelial neoplasia (HGAIN) and 80% or more of anal squamous cell carcinomas [1]. The quadrivalent HPV vaccine (qHPV) (Gardasil, Merck & Co., Inc, Whitehouse Station, NJ) is effective in preventing HPV infection and HPV-related cancers, including cervical, vulvar, vaginal, and anal cancers and their associated precancerous dysplastic lesions [2–4], but it has only been studied in persons without a history of HPV-related disease.

Men who have sex with men (MSM) have high rates of HPV infection, anal cancer, and HGAIN, as well as recurrent neoplasia after treatment. The prevalence of anal HPV infection in human immunodeficiency virus (HIV)–negative MSM ranges from 33% to 57% [5–8]. Unlike women who tend to have a bimodal distribution of cervical HPV infection, the prevalence of anal HPV infection remains constant as MSM age [7, 8]. The rate of anal cancer among HIV-negative MSM is approximately 35 per 100 000 person-years [9], and recurrence in those treated for HGAIN with ablation was 50% within 1 year [10].

Received 9 August 2011; accepted 4 November 2011; electronically published 30 January 2012.

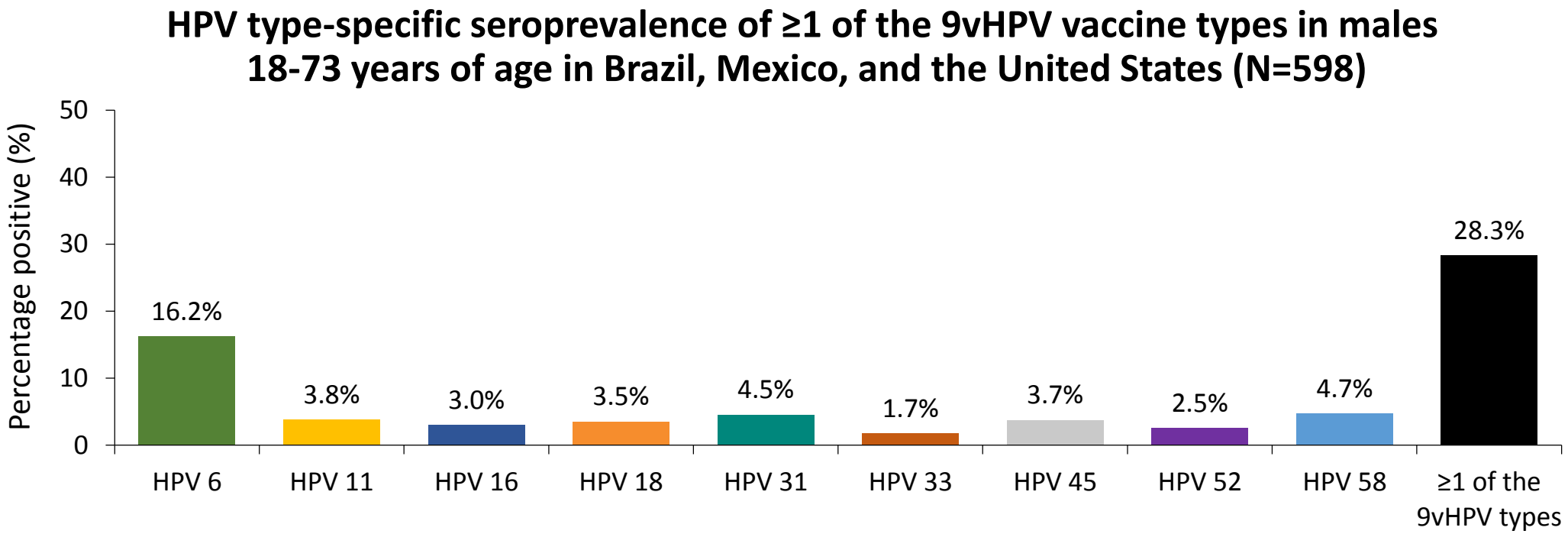
Correspondence: Stephen E. Goldstone, MD, Department of Surgery, Mount Sinai School of Medicine, 420 W 23rd St, Ste PB, New York, NY 10011 (segmd@pmdigy.net).

Clinical Infectious Diseases 2012;54(7):891–8
Published by Oxford University Press on behalf of the Infectious Diseases Society of America 2012.
DOI: 10.1093/cid/cir1036

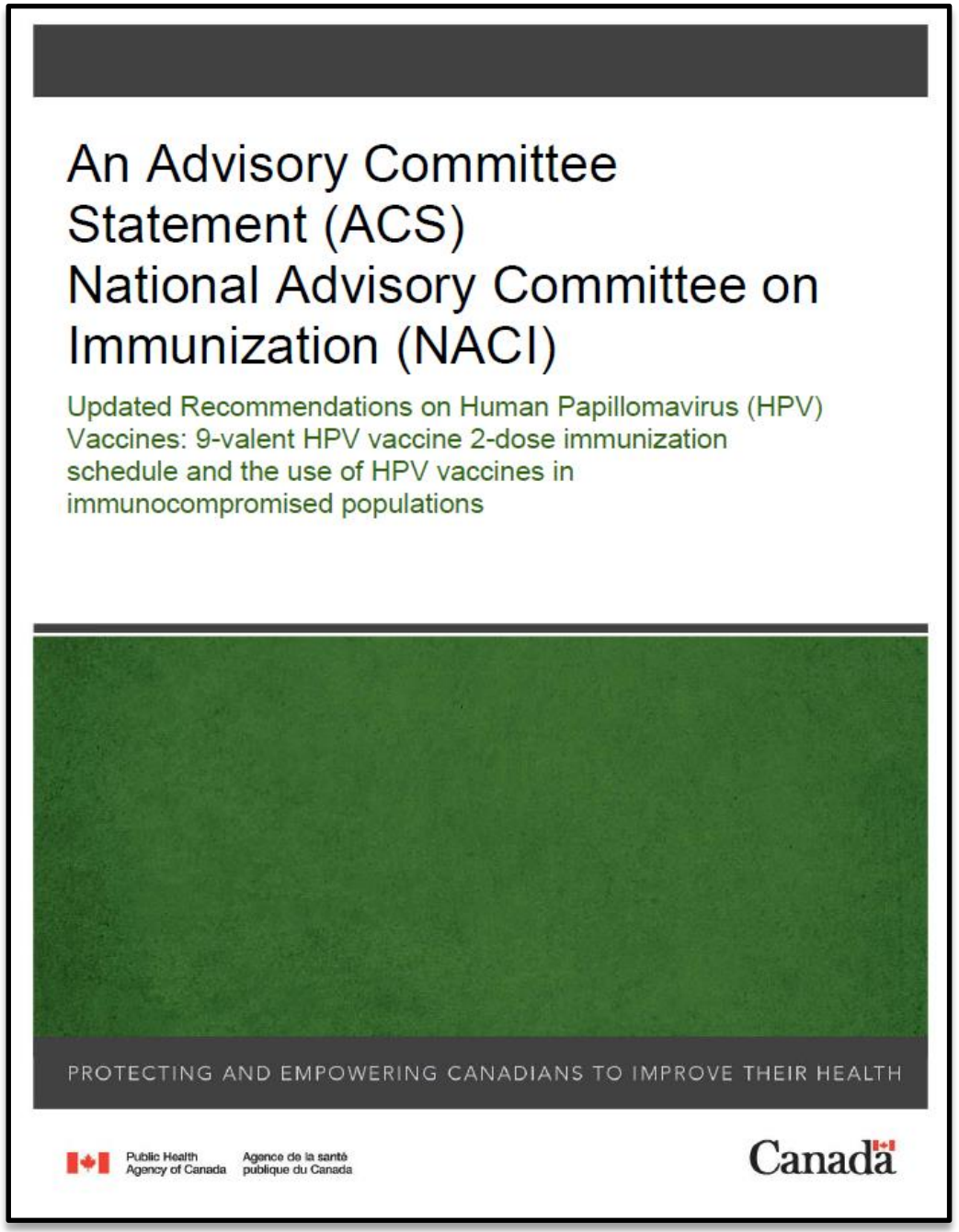


Swedish KA et al. Clin Inf Dis. 2012;54:891–898. MSM: Men Who Have Sex With Men

Most Males Are Not Exposed to All 9 HPV Types



Rahman S et al. PLoS One. 2016;11:e0167173.



NACI and Health Canada recommend HPV vaccination for males and females **who have already had HPV-related** disease because it is safe and offers significant protection against HPV-related diseases related to the genotypes to which they were not exposed

Worldwide Burden of HPV Disease and Role of 9vHPV Vaccine

HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58 are 9 of the most common types found in HPV-related cancers and diseases in males and females[1–6]

Disease Types	**Caused by Types Included in 4vHPV Vaccine** (6/11/16/18)	**Caused by Types Included in 9vHPV Vaccine** (6/11/16/18/31/33/45/52/58)
Cervical cancer cases	70%[1]	90%[1]
Vulvar cancer cases[a]	75%[2]	90%[2]
Vaginal cancer cases[a]	65%[3]	85%[3]
Anal cancer cases[a]	85%[4]	90%–95%[4]
High-grade cervical precancers[a,b]	50%[5]	80%[5]
Low-grade cervical lesions[a]	25%[5]	50%[5]
Genital warts cases	90%[6]	90%[6]

1. de Sanjosé S et al. *Lancet Oncol.* 2010;11:1048–1056. **2.** de Sanjosé S et al. *Eur J Cancer*. 2013;49:3450–3461. **3.** Alemany L et al. *Eur J Cancer*. 2014;50:2846-2854. **4.** Alemany L et al. *Int J Cancer*. 2015;136:98–107. **5.** Joura EA et al. *Cancer Epidemiol Biomarkers Prev*. 2014;23:1997–2008. **6.** Garland SM et al. *J Infect Dis*. 2009;199:805–814. **7.** Guan P et al. *Int J Cancer*. 2012;131:2349–2359.

Efficacy of 9vHPV Vaccine in Females 16-26 Years Old

Articles

Final efficacy, immunogenicity, and safety analyses of a nine-valent human papillomavirus vaccine in women aged 16–26 years: a randomised, double-blind trial

Warner K Huh, Elmar A Joura, Anna R Giuliano, Ole-Erik Iversen, Rosires Pereira de Andrade, Kevin A Ault, Deborah Bartholomew, Ramon M Cestero, Edison N Fedrizzi, Angelica L Hirschberg, Marie-Hélène Mayrand, Angela Maria Ruiz-Sternberg, Jack T Stapleton, Dorothy J Wiley, Alex Ferenczy, Robert Kurman, Brigitte M Ronnett, Mark H Stoler, Jack Cuzick, Suzanne M Garland, Susanne K Kjaer, Oliver M Bautista, Richard Haupt, Erin Moeller, Michael Ritter, Christine C Roberts, Christine Shields, Alain Luxembourg

Summary

Background Primary analyses of a study in young women aged 16–26 years showed efficacy of the nine-valent human papillomavirus (9vHPV; HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58) vaccine against infections and disease related to HPV 31, 33, 45, 52, and 58, and non-inferior HPV 6, 11, 16, and 18 antibody responses when compared with quadrivalent HPV (qHPV; HPV 6, 11, 16, and 18) vaccine. We aimed to report efficacy of the 9vHPV vaccine for up to 6 years following first administration and antibody responses over 5 years.

Methods We undertook this randomised, double-blind, efficacy, immunogenicity, and safety study of the 9vHPV vaccine study at 105 study sites in 18 countries. Women aged 16–26 years old who were healthy, with no history of abnormal cervical cytology, no previous abnormal cervical biopsy results, and no more than four lifetime sexual partners were randomly assigned (1:1) by central randomisation and block sizes of 2 and 2 to receive three intramuscular injections over 6 months of 9vHPV or qHPV (control) vaccine. All participants, study investigators, and study site personnel, laboratory staff, members of the sponsor's study team, and members of the adjudication pathology panel were masked to vaccination groups. The primary outcomes were incidence of high-grade cervical disease (cervical intraepithelial neoplasia grade 2 or 3, adenocarcinoma in situ, invasive cervical carcinoma), vulvar disease (vulvar intraepithelial neoplasia grade 2/3, vulvar cancer), and vaginal disease (vaginal intraepithelial neoplasia grade 2/3, vaginal cancer) related to HPV 31, 33, 45, 52, and 58 and non-inferiority (excluding a decrease of 1·5 times) of anti-HPV 6, 11, 16, and 18 geometric mean titres (GMT). Tissue samples were adjudicated for histopathology diagnosis and tested for HPV DNA. Serum antibody responses were assessed by competitive Luminex immunoassay. The primary evaluation of efficacy was a superiority analysis in the per-protocol efficacy population, supportive efficacy was analysed in the modified intention-to-treat population, and the primary evaluation of immunogenicity was a non-inferiority analysis. The trial is registered with ClinicalTrials.gov, number NCT00543543.

Findings Between Sept 26, 2007, and Dec 18, 2009, we recruited and randomly assigned 14 215 participants to receive 9vHPV (n=7106) or qHPV (n=7109) vaccine. In the per-protocol population, the incidence of high-grade cervical, vulvar and vaginal disease related to HPV 31, 33, 45, 52, and 58 was 0·5 cases per 10 000 person-years in the 9vHPV and 19·0 cases per 10 000 person-years in the qHPV groups, representing 97·4% efficacy (95% CI 85·0–99·9). HPV 6, 11, 16, and 18 GMTs were non-inferior in the 9vHPV versus qHPV group from month 1 to 3 years after vaccination. No clinically meaningful differences in serious adverse events were noted between the study groups. 11 participants died during the study follow-up period (six in the 9vHPV vaccine group and five in the qHPV vaccine group); none of the deaths were considered vaccine-related.

Interpretation The 9vHPV vaccine prevents infection, cytological abnormalities, high-grade lesions, and cervical procedures related to HPV 31, 33, 45, 52, and 58. Both the 9vHPV vaccine and qHPV vaccine had a similar immunogenicity profile with respect to HPV 6, 11, 16, and 18. Vaccine efficacy was sustained for up to 6 years. The 9vHPV vaccine could potentially provide broader coverage and prevent 90% of cervical cancer cases worldwide.

Funding Merck & Co, Inc.

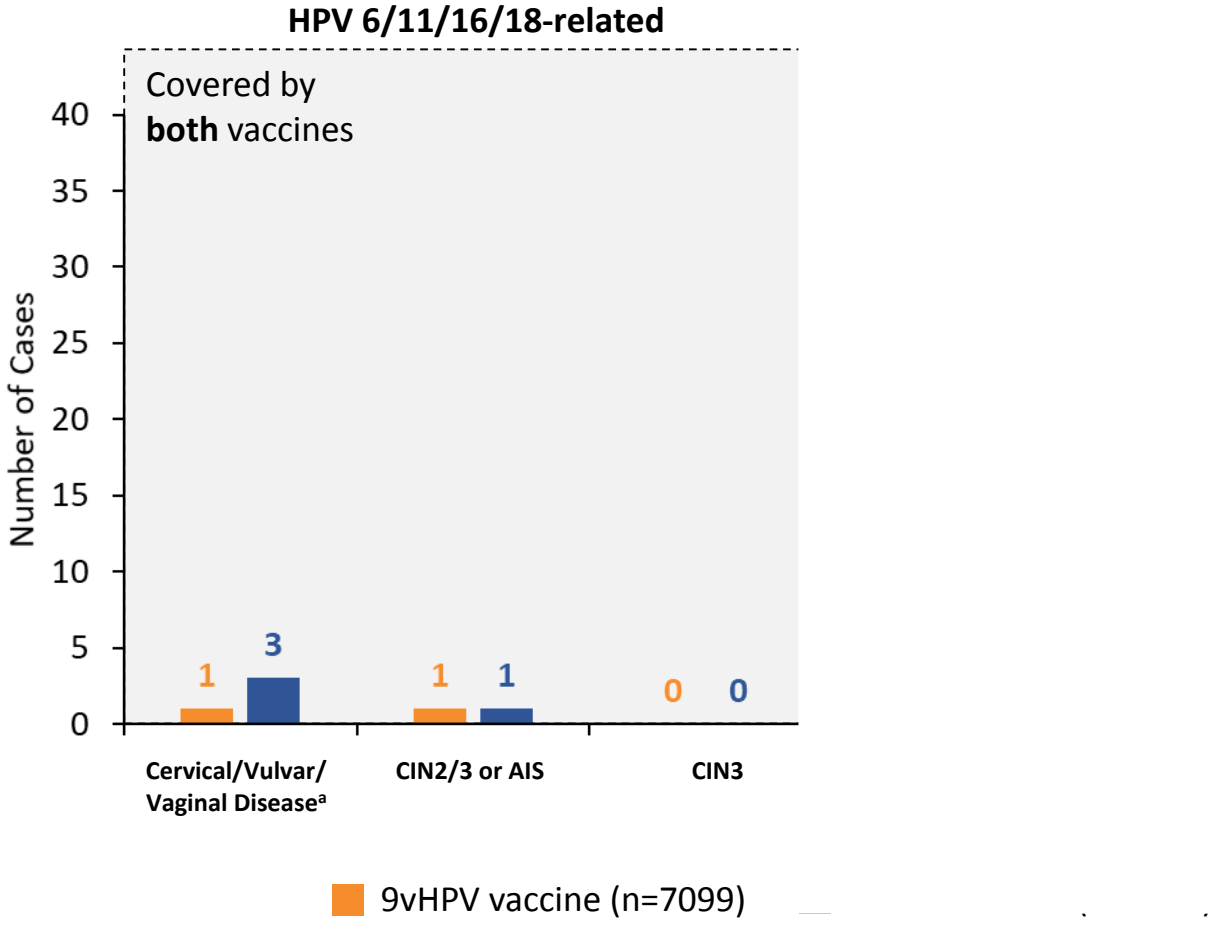
Introduction

Human papillomavirus (HPV) infection causes benign, precancerous, and malignant disease, localised primarily in the anogenital area and upper airway, including cancers and precancers of the cervix, vulva, vagina, anus, penis, tonsil, and base of the tongue.[1] HPV infection can also cause anogenital warts and recurrent respiratory papillomatosis.[1] Available HPV vaccines, including the bivalent HPV 16 and 18 L1 virus-like particle vaccine and the quadrivalent HPV 6, 11, 16, and 18 L1 virus-like particle (qHPV) vaccine, prevent infection and disease related to oncogenic HPV 16 and 18.[2] HPV 16 and 18 are

Published Online September 5, 2017 http://dx.doi.org/10.1016/S0140-6736(17)31821-4

See Online/Comment http://dx.doi.org/10.1016/S0140-6736(17)32144-X

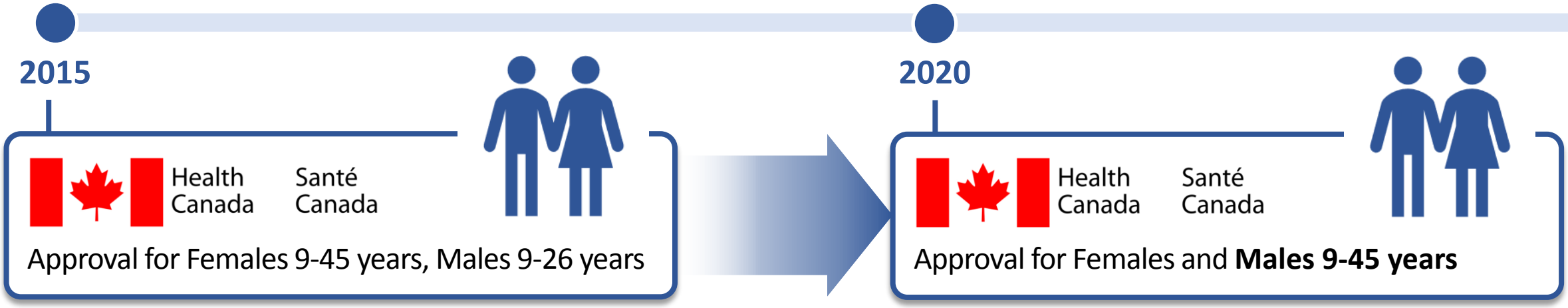
Division of Gynecologic Oncology, University of Alabama at Birmingham, Birmingham, AL, USA (W K Huh MD); Department of Gynecology, Comprehensive Cancer Center, Medical University of Vienna, Vienna, Austria (E A Joura MD); Center for Infection Research in Cancer, Moffitt Cancer Centre, Tampa, FL, USA (A R Giuliano PhD); Department of Clinical Science, University of Bergen, Bergen, Norway (O-E Iversen MD); Department of Gynecology and Obstetrics, Haukeland University Hospital, Bergen, Norway (O-E Iversen); CERHFAC/Universidade Federal do Paraná, Setor de Ciências da Saúde, Departamento de Tocoginecologia, Paraná, Brazil (R P de Andrade MD); Department of Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, KS, USA (K A Ault MD); Department of Obstetrics and Gynecology, The Ohio State University/Wexner Medical Center, Columbus, OH, USA (D Bartholomew MD); Department of Obstetrics and Gynecology, University of California Irvine School of Medicine, UC Irvine Health Orange, CA, USA (R M Cestero MD); Department of Obstetrics and Gynecology of The Federal University of Santa Catarina, Santa Catarina, Brazil (E N Fedrizzi M D); Department of Obstetrics and Gynecology, Karolinska University Hospital, Stockholm, Sweden (A L Hirschberg MD);



[a]Includes CIN 2/3, AIS, cervical cancer, VIN 2/3, VaIN 2/3, vulvar cancer, and vaginal cancer.
AIS: adenocarcinoma in situ; CIN: cervical intraepithelial neoplasia; VaIN: vaginal intraepithelial neoplasia; VIN: vulvar intraepithelial neoplasia;

Huh WK et al. Lancet. 2017 Nov 11;390(10108):2143-2159.

Health Canada Approval of 9vHPV Vaccine



- Additional 5 serotypes confer protection against additional 5-30% of anogenital cancers and HPV diseases not covered by 2vHPV and 4vHPV vaccines
- Used in schools and provincially-funded public programs
  (July 1, 2020 Alberta expanded provincial coverage to include all males and females <27 years old)
- 3-dose schedule 0, 2, 6m if > 15 years old with optimal benefit if vaccinated prior to HPV infection

https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-9-human-papillomavirus-vaccine.html

New US FDA Approval of 9vHPV Vaccine For Prevention of Head & Neck Cancers

- On June 12, 2020, the 9-valent HPV vaccine received accelerated approval in the United States for the **prevention of oropharyngeal and other head & neck cancers** caused by HPV types 16, 18, 33, 45, 52, and 58.
    - randomized, placebo-controlled confirmatory trial (V503-049; NCT04199689) to confirm the anticipated clinical benefit of the 9vHPV vaccine in preventing persistent oral HPV infection in males 20-45 years of age (initiated in Feb 2020)

https://www.fda.gov/vaccines-blood-biologics/vaccines/gardasil-9

Currently no HPV vaccines outside of the US are approved for the prevention of oropharyngeal cancer and other head & neck cancers caused by HPV types 16, 18, 33, 45, 52, and 58.

Consensus Amongst Global Health Authorities on HPV Vaccine Safety

- To date, no safety concerns for the use of 4v HPV vaccine have arisen from ongoing surveillance studies in females and males (>270 million doses administered worldwide)
- Most common side effects are pain (90%), redness (34%), and swelling (40%)
- Clusters of post-vaccination syndromes and deaths have been investigated with no causal association with HPV vaccines
- Global Advisory Committee on Vaccine Safety 2017 found no new adverse events of concern and HPV vaccines are extremely safe

1. Harrington T. Presented at: National Foundation of Infectious Diseases 15th Annual Conference on Vaccine Research; 7-9 May, 2012; Baltimore, MD. Presentation 3B; 2. Gee J. Presented at: Advisory Committee on Immunization Practices Meeting; October 25, 2011; Atlanta, GA. 3. Food and Drug Administration (FDA) [last modified 2012 May 20; cited 2015 Mar 18]. 4. Global Advisory Committee on Vaccine Safety, 17-18 December 2008. Wkly Epidemiol Rec. 2009;84:37-40. 5. European Medicines Agency (EMA) [last modified 2011; cited 2012 Mar 21]. 6. ECDC Guidance 2012 last modified 2012; [cited 2012 Sept 24].

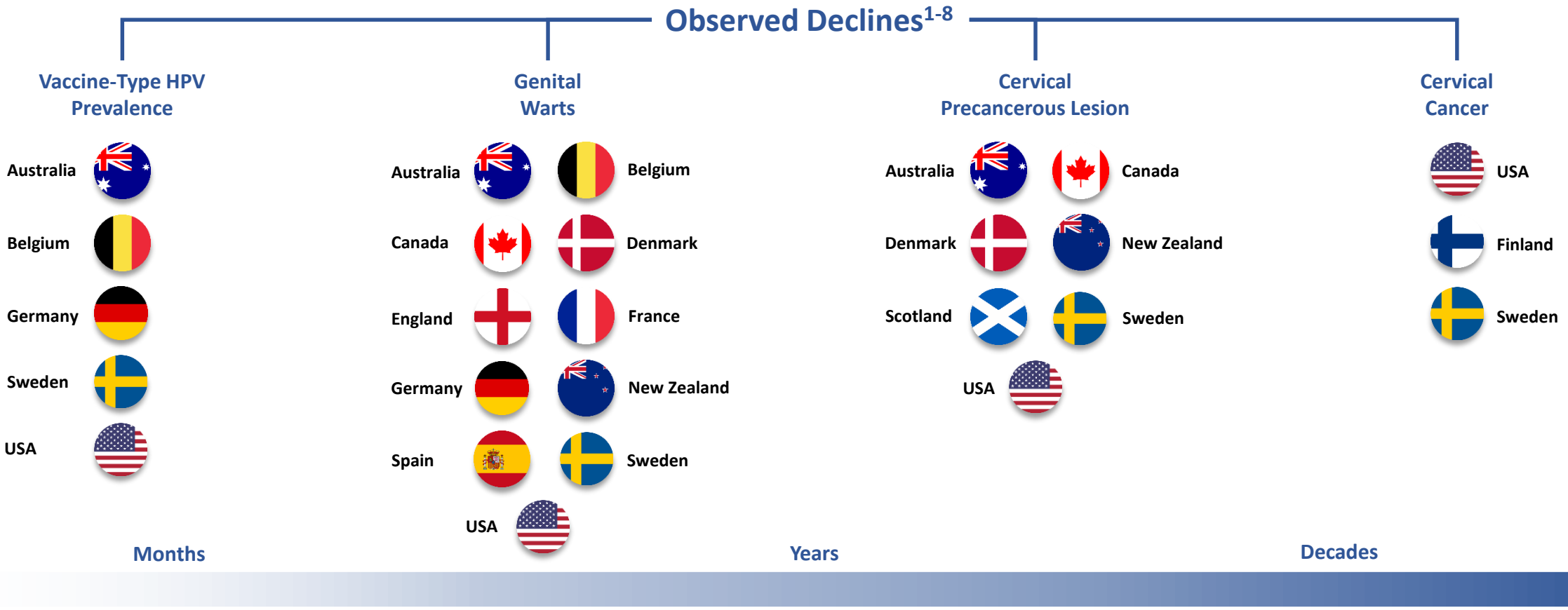
National Advisory Committee on Immunization (NACI) Recommendations for HPV Vaccination in Canada

Females	**2v, 4v or 9v HPV vaccine is recommended for females:** ▪ **9-26 years of age** for routine vaccination ▪ May be administered to **females over 26 years of age** who have not been vaccinated previously or who have not completed the series
Males	**4v or 9v HPV vaccines is recommend for males:** ▪ **9-26 years of age** for routine vaccination ▪ May be administered to **males over 26 years of age** who have not been vaccinated previously or who have not completed the series
General	▪ 2v and 4v HPV vaccine may be administered to immunocompetent individual **9-14** years of age using **either a 2-dose or 3-dose schedule** ▪ Any immunocompromised individual, immunocompetent HIV infected individuals and individuals who have not receive any dose of HPV vaccine by **15** years of age should continue to receive **three doses of HPV vaccine** ▪ There is **insufficient evidence** at this time to **recommend**, at a population level, **re-immunization with 9v HPV** vaccine in individuals who have completed an immunization series with another HPV vaccine.

Note that the NACI recommendations **do not have an upper age limit** for vaccination of males or females

Public Health Agency of Canada. An advisory committee statement (ACS) National Advisory Committee on Immunization. Updated recommendation on human papillomavirous (HPV) vaccines: 9-valent HPV vaccine and clarification of minimum intervals between doses in the HPV immunization schedule.

Real-world Evidence With HPV Vaccination



1. Garland et al. Clin Infect Dis. 2016 Aug 15;63(4):519-27.; 2. Checchi et al. Sex Transm Infect. 2019 Aug;95(5):368-373.; 3. Palmer et al. BMJ. 2019 Apr 3;365:l1161.; 4. Innes et al. N Z Med J. 2020 Jan 17;133(1508):72-84.; 5. Brotons et al. Prev Med. 2020 Sep;138:106166. 6. Guo et al. Am J Prev Med. 2018. Aug;55(2):197-204.; 7. Luostarinen T, et al. Int J Cancer. 2018. May 15;142(10):2186-2187.; 8. Lei J, et al. N Engl J Med. 2020. Oct 1;383(14):1340-1348.

Real-world Evidence With HPV Vaccination

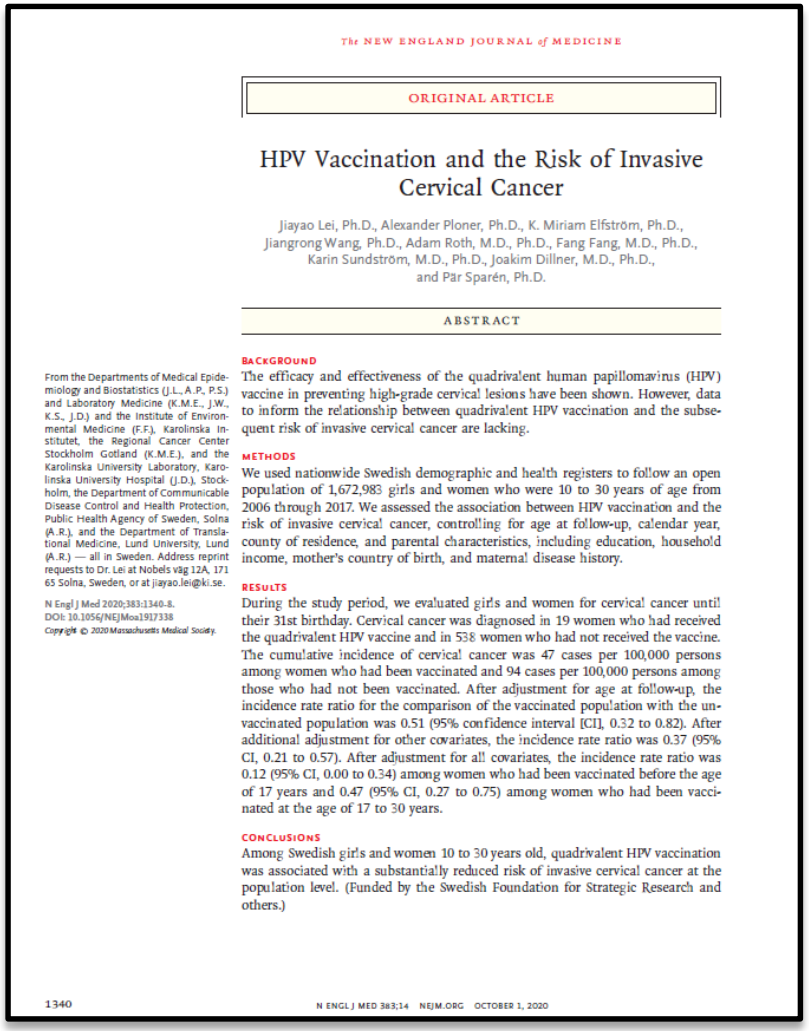
% of Reduction[1-8]	Australia	Belgium	Canada	Denmark	England	France	Germany	New Zealand	Scotland	Sweden	USA
Genital Warts	96%*	72%	43%*	95%	82%	47%	60%	63%		92%	61%
Cervical Abnormalities CIN2+	66%*		86%	40%					88%	75%	94%

*Statistical significance was either not assessed or not reached. CIN = cervical intraepithelial neoplasia

Differences in impact more likely reflect variations in target population, coverage rate, and duration of follow-up rather than fundamental differences in vaccine effectiveness[1]

1. Garland et al. Clin Infect Dis. 2016 Aug 15;63(4):519-27.; 2. Checchi et al. Sex Transm Infect. 2019 Aug;95(5):368-373.; 3. Palmer et al. BMJ. 2019 Apr 3;365:l1161.; 4. Innes et al. N Z Med J. 2020 Jan 17;133(1508):72-84.; 5. Brotons et al. Prev Med. 2020 Sep;138:106166. 6. Guo et al. Am J Prev Med. 2018. Aug;55(2):197-204.; 7. Luostarinen T, et al. Int J Cancer. 2018. May 15;142(10):2186-2187.; 8. Lei J, et al. N Engl J Med. 2020. Oct 1;383(14):1340-1348.

4vHPV Vaccination Substantially Reduces the Risk of Invasive Cervical Cancer



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

HPV Vaccination and the Risk of Invasive Cervical Cancer

Jiayao Lei, Ph.D., Alexander Ploner, Ph.D., K. Miriam Elfström, Ph.D., Jiangrong Wang, Ph.D., Adam Roth, M.D., Ph.D., Fang Fang, M.D., Ph.D., Karin Sundström, M.D., Ph.D., Joakim Dillner, M.D., Ph.D., and Pär Sparén, Ph.D.

From the Departments of Medical Epidemiology and Biostatistics (J.L., A.P., P.S.) and Laboratory Medicine (K.M.E., J.W., K.S., J.D.) and the Institute of Environmental Medicine (F.F.), Karolinska Institutet, the Regional Cancer Center Stockholm Gotland (K.M.E.), and the Karolinska University Laboratory, Karolinska University Hospital (J.D.), Stockholm, the Department of Communicable Disease Control and Health Protection, Public Health Agency of Sweden, Solna (A.R.), and the Department of Translational Medicine, Lund University, Lund (A.R.) — all in Sweden. Address reprint requests to Dr. Lei at Nobels väg 12A, 171 65 Solna, Sweden, or at jiayao.lei@ki.se.

N Engl J Med 2020;383:1340-8.
DOI: 10.1056/NEJMoa1917338

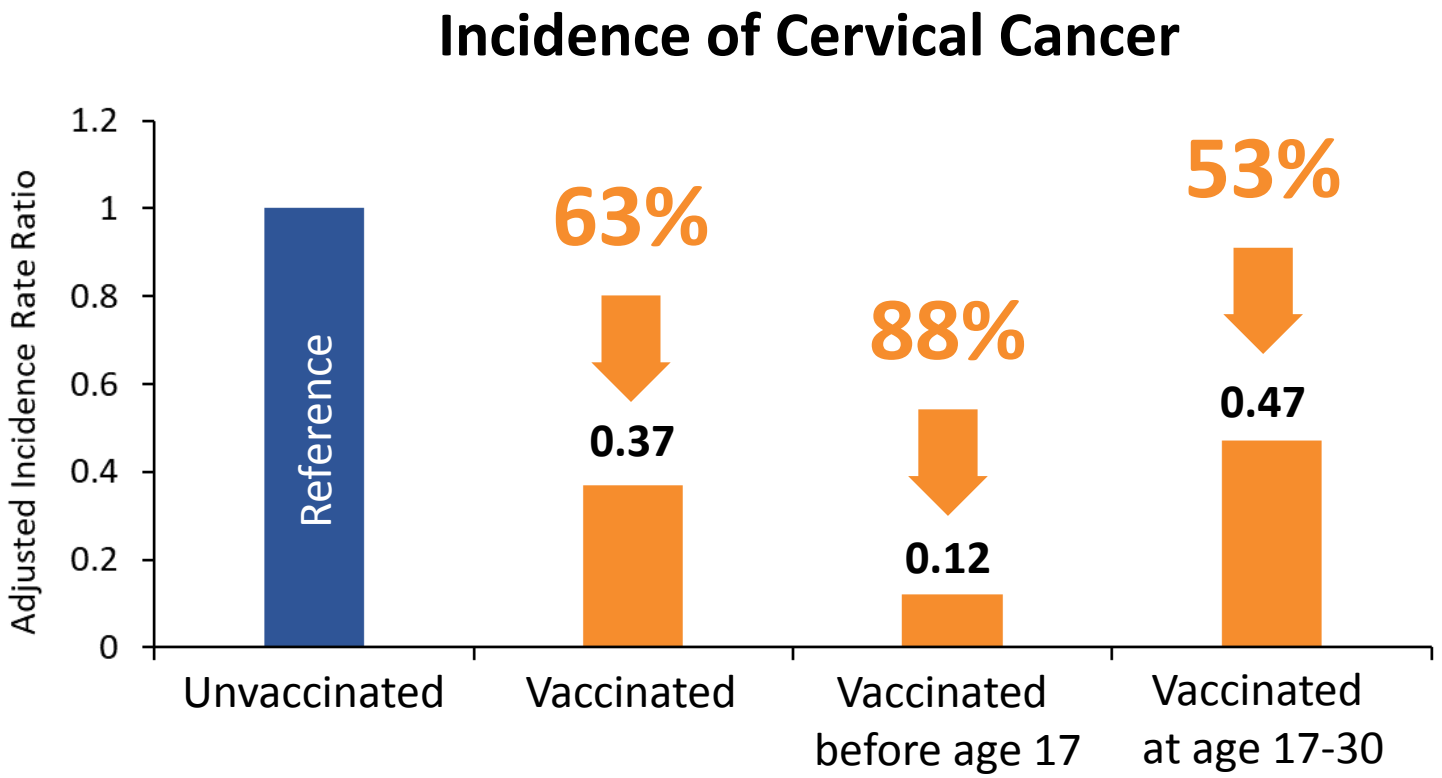
ABSTRACT

BACKGROUND
The efficacy and effectiveness of the quadrivalent human papillomavirus (HPV) vaccine in preventing high-grade cervical lesions have been shown. However, data to inform the relationship between quadrivalent HPV vaccination and the subsequent risk of invasive cervical cancer are lacking.

METHODS
We used nationwide Swedish demographic and health registers to follow an open population of 1,672,983 girls and women who were 10 to 30 years of age from 2006 through 2017. We assessed the association between HPV vaccination and the risk of invasive cervical cancer, controlling for age at follow-up, calendar year, county of residence, and parental characteristics, including education, household income, mother's country of birth, and maternal disease history.

RESULTS
During the study period, we evaluated girls and women for cervical cancer until their 31st birthday. Cervical cancer was diagnosed in 19 women who had received the quadrivalent HPV vaccine and in 538 women who had not received the vaccine. The cumulative incidence of cervical cancer was 47 cases per 100,000 persons among women who had been vaccinated and 94 cases per 100,000 persons among those who had not been vaccinated. After adjustment for age at follow-up, the incidence rate ratio for the comparison of the vaccinated population with the unvaccinated population was 0.51 (95% confidence interval [CI], 0.32 to 0.82). After additional adjustment for other covariates, the incidence rate ratio was 0.37 (95% CI, 0.21 to 0.57). After adjustment for all covariates, the incidence rate ratio was 0.12 (95% CI, 0.00 to 0.34) among women who had been vaccinated before the age of 17 years and 0.47 (95% CI, 0.27 to 0.75) among women who had been vaccinated at the age of 17 to 30 years.

CONCLUSIONS
Among Swedish girls and women 10 to 30 years old, quadrivalent HPV vaccination was associated with a substantially reduced risk of invasive cervical cancer at the population level. (Funded by the Swedish Foundation for Strategic Research and others.)



Lei J, et al. N Engl J Med. 2020. Oct 1;383(14):1340-1348.

Dr Tedros Adhanom Ghebreyesus,
WHO Director-General

WHO calls for “coordinated action globally to eliminate cervical cancer” May 19, 2018

Cervical cancer is one of the most preventable and treatable forms of cancer as long as it is prevented with HPV vaccination, detected early, and managed effectively.

Cervical cancer remains one of the gravest threats to women’s lives, and globally, one woman dies of cervical cancer every two minutes. This suffering is unacceptable, and cannot continue.

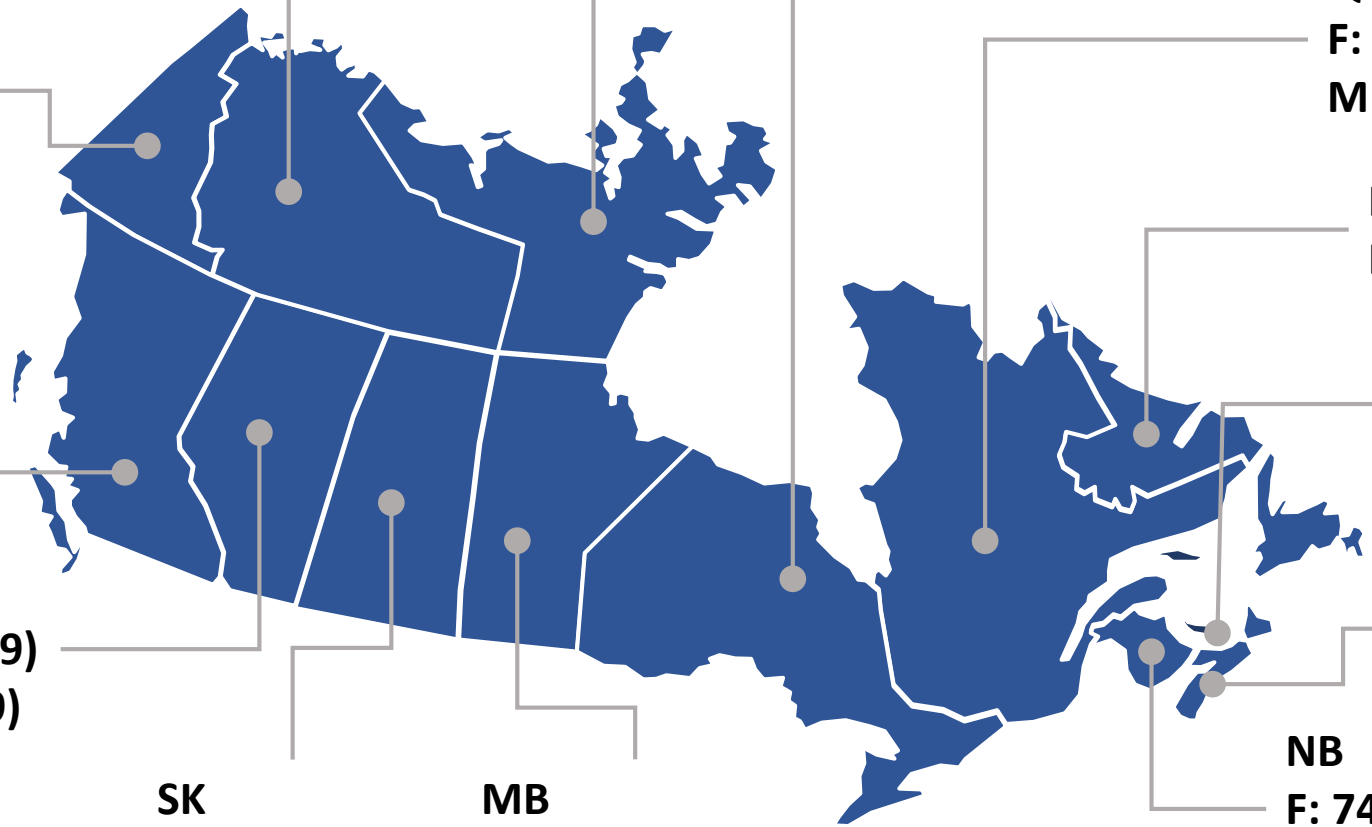
HPV vaccines are truly wonderful inventions.

If only we had vaccines against every form of cancer.

“Elimination is within reach”

Canada Responds: Ending cervical cancer in Canada is possible

School-based HPV Vaccination Uptake in Canada



NT
F: 55% (2016-2017)

NU
N/A

ON
F: 62.4% (2017-2018)
M: 57.5% (2017-2018)

QC
F: 79% (2018-2019)
M: 77% (2018-2019)

YT
F: 66.5% (2015-2016)

NL
F: 92% (2015-2016)

BC
F: 66.1% (G6, 2019)
M: 63.5% (G6, 2019)

PEI
F: 84.3% (2015-2016)
M: 85% (2015-2016)

NS
F: 73.4% (2016-2017)
M: 84.9% (2016-2017)

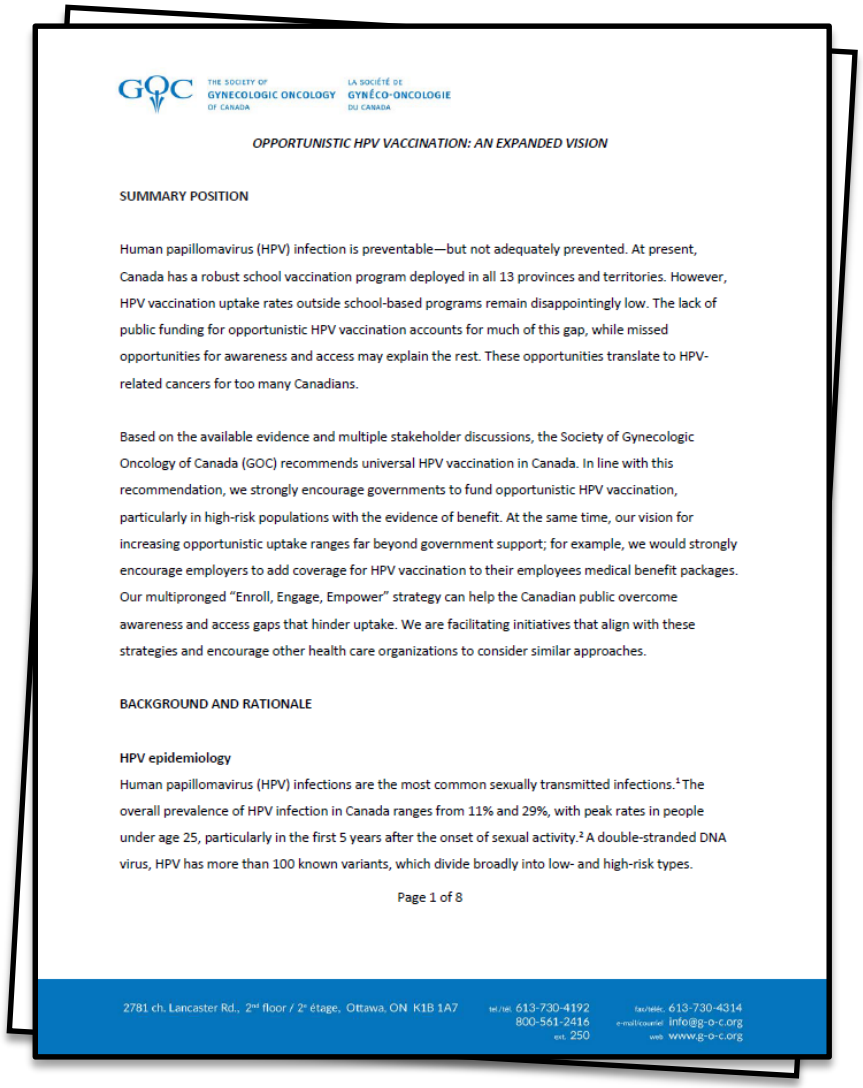
AB
F: 65.6% (by age 12, 2019)
M: 63% (by age 12, 2019)

NB
F: 74.9% (2018-2019)
M: 72.8% (2018-2019)

SK
F: 69% (2017)

MB
F: 69.4% (2017)

Low Adult HPV Vaccination Uptake in Canada



GOC THE SOCIETY OF GYNECOLOGIC ONCOLOGY OF CANADA / LA SOCIÉTÉ DE GYNÉCO-ONCOLOGIE DU CANADA

OPPORTUNISTIC HPV VACCINATION: AN EXPANDED VISION

SUMMARY POSITION

Human papillomavirus (HPV) infection is preventable—but not adequately prevented. At present, Canada has a robust school vaccination program deployed in all 13 provinces and territories. However, HPV vaccination uptake rates outside school-based programs remain disappointingly low. The lack of public funding for opportunistic HPV vaccination accounts for much of this gap, while missed opportunities for awareness and access may explain the rest. These opportunities translate to HPV-related cancers for too many Canadians.

Based on the available evidence and multiple stakeholder discussions, the Society of Gynecologic Oncology of Canada (GOC) recommends universal HPV vaccination in Canada. In line with this recommendation, we strongly encourage governments to fund opportunistic HPV vaccination, particularly in high-risk populations with the evidence of benefit. At the same time, our vision for increasing opportunistic uptake ranges far beyond government support; for example, we would strongly encourage employers to add coverage for HPV vaccination to their employees medical benefit packages. Our multipronged "Enroll, Engage, Empower" strategy can help the Canadian public overcome awareness and access gaps that hinder uptake. We are facilitating initiatives that align with these strategies and encourage other health care organizations to consider similar approaches.

BACKGROUND AND RATIONALE

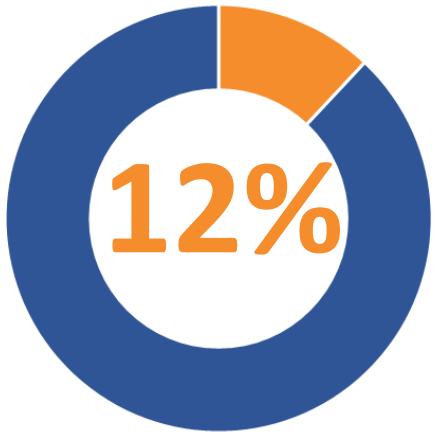
HPV epidemiology

Human papillomavirus (HPV) infections are the most common sexually transmitted infections.[1] The overall prevalence of HPV infection in Canada ranges from 11% and 29%, with peak rates in people under age 25, particularly in the first 5 years after the onset of sexual activity.[2] A double-stranded DNA virus, HPV has more than 100 known variants, which divide broadly into low- and high-risk types.

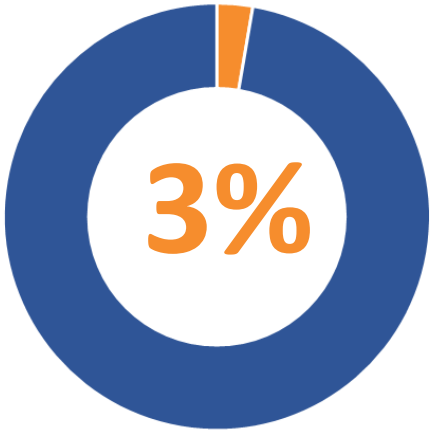
Page 1 of 8

2781 ch. Lancaster Rd., 2nd floor / 2e étage, Ottawa, ON K1B 1A7 tel/tél: 613-730-4192 800-561-2416 ext. 250 fax/téléc: 613-730-4314 e-mail/courriel: info@g-o-c.org web: www.g-o-c.org

2014 **8.3%** females 27-45y received at least 1 dose



Uptake Rate in 27-31 Years Old



Uptake Rate in 42-46 Years Old

- Lack of knowledge of value of vaccination >26 years old
- Gap in physician-patient communication and physician education

https://g-o-c.org/wp-content/uploads/2015/01/18_EEE_WhitePaper_FINAL_Jun18.pdf

Barriers to HPV Vaccination in Canada

Physicians' Perspectives[1]

#1 Cost of HPV Vaccine

***92-95% of physicians: Cost** #1 barrier*
*Perceived barriers of cost may **limit recommendations for vaccination**, particularly among older women or men.*

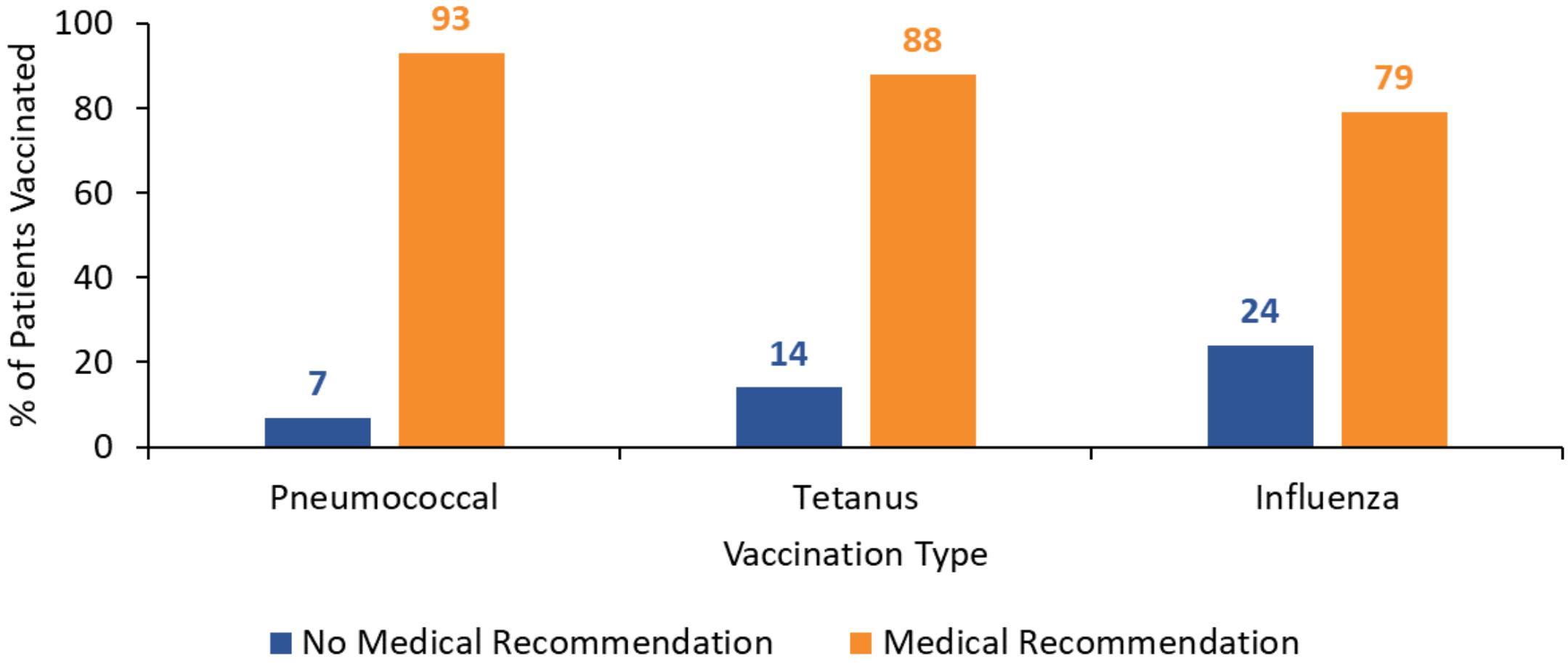
Public Perspectives[2]

#1 Lack of Physician Recommendation

*The number one reported barrier to vaccination for the general public was **not having a recommendation from a doctor**. **Cost** was seen as a barrier by **only 18% (male)** and **20% (female)** of participants.*

1. Steben M et al. J Obstet Gynaecol Can. 2019 May;41(5):599-607.e3.; 2. Steben M et al. J Obstet Gynaecol Can. 2019 Aug;41(8):1125-1133.e6.

Impact of Healthcare Professional's Recommendation on Patient Acceptance of Vaccination



Environics Research Group. Canadian Adult National Immunization Coverage (Adult NICS) Survey. Final Report. Ottawa, ON; 2006 Nov.

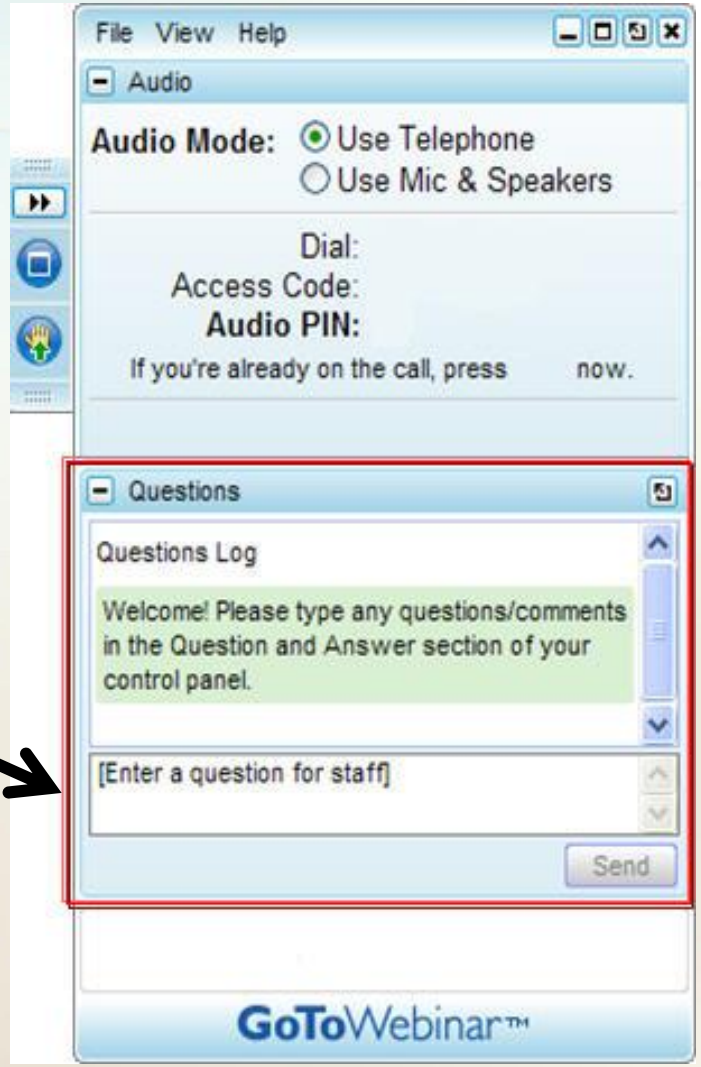
Summary: Many Reasons to Vaccinate Adults

- Males are susceptible to HPV infections and diseases throughout their lifetime
- Reinfection and recurrent disease are common in males
- HPV vaccines are safe, effective, and recommended by NACI for males and females >9 years old with no upper age limit regardless of past HPV exposure
- A reduction in HPV prevalence and diseases has been demonstrated amongst males and females who received the HPV vaccine
- Let's "do our part" in the fight against HPV by educating and strongly recommending HPV vaccines for everyone

Global Strategy to Accelerate Elimination of Cervical Cancer

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/PH8C3RW

- **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, CIDC GWurtak@CIDCgroup.org

This educational program is made possible through the support of **Merck Canada Inc.** and with assistance by BD Diagnostics and Immunize Canada